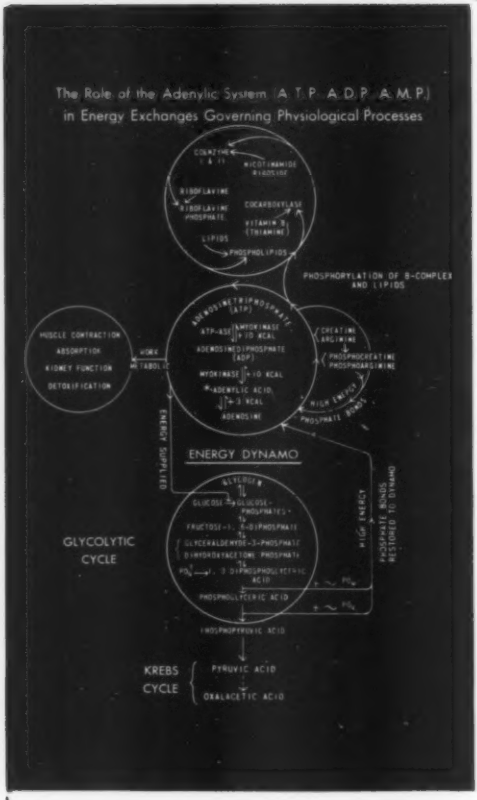
Neurology

OFFICIAL JOURNAL OF
THE AMERICAN ACADEMY OF NEUROLOGY

JUNE - 1956
Volume 6 — Number 6



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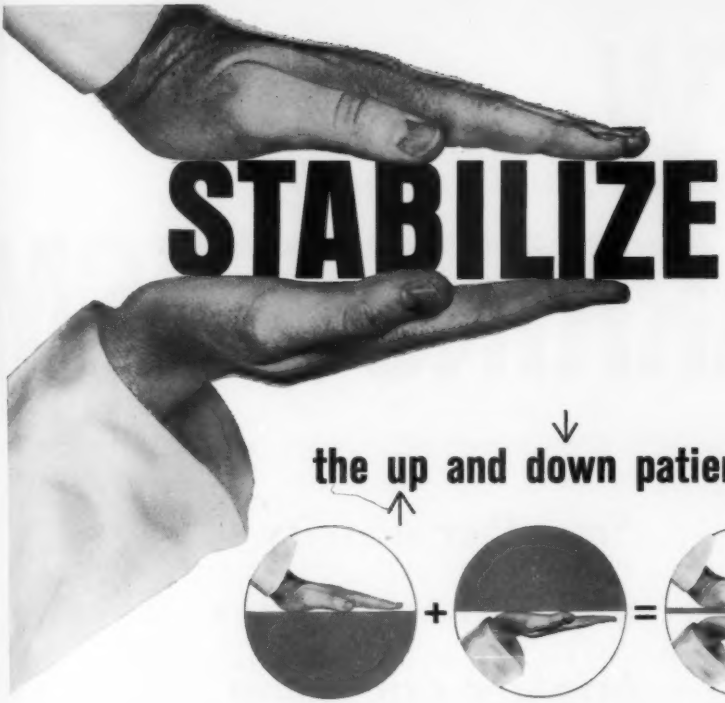

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1. Arnoff, B.: Personal communication. 2. Lazarte, J. A., and Petersen, M.C.: Personal communication.

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NEUROLOGY is published monthly at 84 South Tenth Street, Minneapolis 3, Minnesota, by LANCET PUBLICATIONS, INCORPORATED. Subscription rate: $12.00 a year, $1.00 a copy; outside the United States $13.00 a year, $1.10 a copy. Entered as second class matter at the postoffice at Minneapolis, January 23, 1951.

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1. Livingston, S., and Petersen, D.: New England J. Med. *254*:327 (Feb. 16) 1956.
2. Pence, L. M.: Texas State J. Med. *50*:290 (May) 1954.
3. Berman, B. A.: Am. J. Psychiat. *112*:541 (Jan.) 1956.

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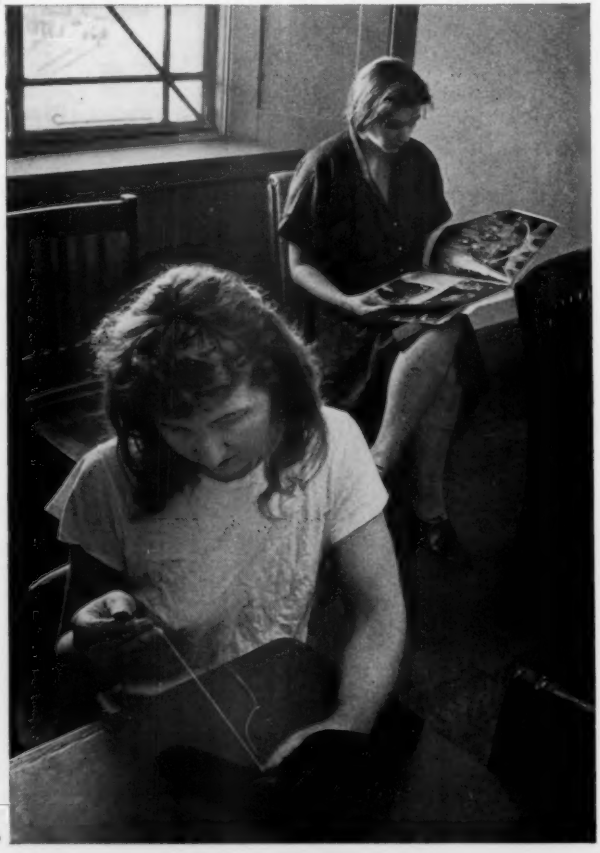

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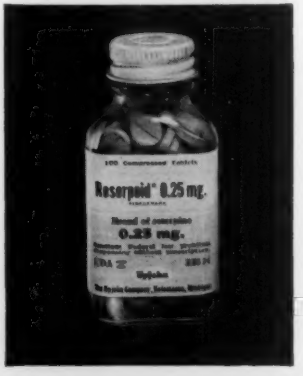

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Volume 6 Neurology Number 6

Electrophysiologic and Clinical Observations in Hemifacial Spasms

Andre A. Weil, M.D. and William A. Nosik, M.D

HEMIFACIAL SPASMS have been observed[1] as an accessory symptom in a variety of neurologic disorders such as purulent meningitis, trigeminal neuralgia, and tetanus. Following the great epidemic of encephalitis in 1920 various authors[2,3] reported hemifacial spasms in verified lesions of the basal ganglia; in animals motor manifestations in the face following irritation of the mesencephalon and diencephalon are not uncommon.[4] Hemifacial spasms of this type, however, are accompanied by additional neurologic signs and symptoms of systemic or regional origin, as they may also be observed in hemifacial spasms occurring in cerebellopontine tumors,[5] arachnoiditis of the posterior fossa,[6] and aneurysms of the basilar artery.[7] Before the turn of the century the theory of reflex irritation by trigeminal nerve disturbances was in vogue,[8] but the advancement of neurosurgery demonstrated that section of the trigeminal nerve does not alter preexisting hemifacial spasms.[9,10]

We are concerned with the occurrence of hemifacial spasm as an apparently isolated neurologic or psychoneurologic phenomenon. Even before Brissaud and co-workers[11] in 1906 tried to differentiate psychogenic forms (tics) from nonpsychogenic forms (spasms), there was a good deal of discrepancy in the literature about the etiology of these facial dyskinesias. However, Gowers[12] in 1888 had already given a good description of hemifacial spasms, trying to differentiate them from tic movements. Contrary to this, Dana[13] stated in 1925 that "there is usually a neuropathic constitution" in facial spasms and this concept was reiterated by Andre-Thomas

From the department of neurology, Western Reserve University (City Hospital, Cleveland), Cleveland Receiving Hospital, and Huron Road Hospital, E. Cleveland, Ohio, and from the department of neurosurgery, Huron Road Hospital, St. Luke's Hospital, and University Hospitals, Cleveland, Ohio.

Read at the ninth annual meeting of the American Electroencephalographic Society, June 11, 1955, Chicago.

and DeAjuriaguerra[14] in 1949. In 1913 Buzzard[15] mentioned that the disturbance lies in the facial nucleus of the pons, a concept that was also advocated by Ehni and Woltman[9] in 1945 and by Wartenberg[16] in his monograph of 1952.

Considering the discrepancies in clinical opinion about the origin, classification, and subsequent therapeutic approach of hemifacial spasms, it is strange to note that clinicians have not sought the help of electrophysiologic procedures to clarify this problem. However, Thiebaut and co-workers[17] examined 12 patients with hemifacial spasms electromyographically and differentiated them into "idiopathic" and "postparalytic" groups. They stressed the repetitive character of "firing" which in "postparalytic cases appeared to be superimposed on a constant background activity consisting in the pulsation of a motor unit. . . . The 'idiopathic' spasm, even though characterized by an important paretic element, is nevertheless clearly distinguishable from the postparalytic spasm, since the latter displays a regular spontaneous infraclinical activity which is absent in the former."

This paper does not propose to be a research study of the problem of hemifacial spasms, but should rather be considered a practical clinical approach toward better understanding, classification, and treatment of facial twitchings. With the help of careful clinical observations, standard neurologic tools, and an inkwriter oscillograph (utilizing both standard electroencephalographic electrodes and coaxial needle electrodes), hemifacial spasms have been classified into three groups: 1) hemifacial spasms due to cortical irritation, 2) due to nuclear "firing," and 3) due to psychogenic conversion reactions (habit spasms).

HEMIFACIAL SPASMS DUE TO CORTICAL IRRITATION

Wartenberg[16] has stated that in rare instances a minute, irritating focus in the cortical facial center may produce a clinical picture similar to hemifacial spasm. Klimke[18] has also reported cases of this kind. It is common neurosurgical knowledge that facial twitchings can be produced by stimulating the contralateral, precentral face area; Penfield and Jasper[19] reproduced these dyskinesias even by stimulating the supplementary motor area within the interhemispheral fissure. We observed only two patients in whom hemifacial spasms could be attributed to cortical irritation.

A 77 year old white woman sustained a cerebral contusion 12 years ago, manifested originally by weakness in the left arm and twitching in the left face. Although the weakness disappeared, the twitchings of the left face persisted, the lower facial muscles being involved first. The discharges showed a mixture of tonic contractions occasionally resembling clonic dyskinesias, and occasionally fasciculations spreading from the orbicularis oris to orbicularis oculi, frontalis, and auriculotemporal muscle groups. No electromyogram was obtained, but the electroencephalogram showed rhythmic repetitive left frontal spikes during a clonic spasm of the left frontal muscle (figure 1A); irregular, bi-phasic spikes were noted during fasciculatory movements, apparently coming from the left auriculotemporal muscle groups. Sharp wave patterns in the theta frequencies interrupted the cortical rhythmicity over the right anterior temporal derivation (figure 1B). Even when no facial movements were noticeable, isolated spikes appeared over the left frontal electrode placement which could have had either muscular or cerebral origin and which were interspersed by dissociated, low voltage, right frontal theta pattern in the electroencephalogram (figure 1C. Note the entirely different wave contour of "blink" artifacts).

The second patient observed was a white man in his eighties who showed left facial clonic spasms with pyramidal signs on the left,

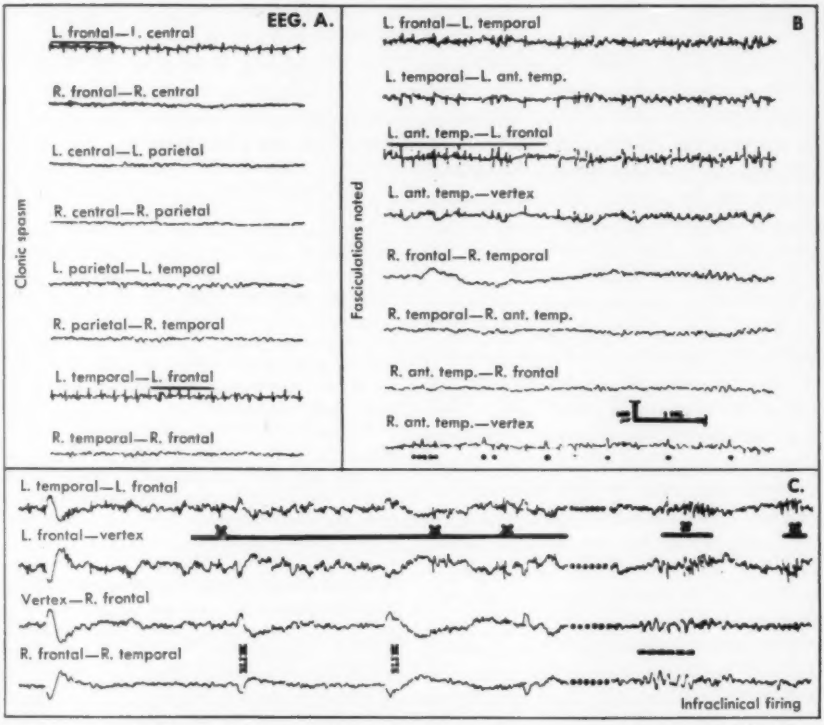

FIG. 1. Hemifacial spasm due to cortical irritation in a 77 year old woman. *A.* Repetitive left frontal spikes of muscular origin (heavy line). *B.* Biphasic spikes over left anterior temporal-left frontal electrode derivation derived from left auriculotemporal muscle groups (heavy line). *C.* Left frontal spikes of either muscular or cerebral origin (heavy line); right frontal theta pattern (dotted line).

believed to be due to a cerebrovascular occlusive lesion of arteriosclerotic etiology.

Comment. Hemifacial spasms due to cortical irritation appear to be uncommon. Some additional neurologic signs and symptoms due to involvement of adjacent cortical areas seem to accompany the hemifacial spasms, at least originally. Electrophysiologic abnormalities in the one case so examined included repetitive and single spike firing, apparently coming from the frontalis and auriculotemporal muscle groups. These were observed even without visible evidence of any hemifacial spasm and furthermore showed actual disturbances of cerebral rhythmicity. Neurosurgical treatment or anticonvulsant medication is indicated in these cases.

HEMIFACIAL SPASMS DUE TO NUCLEAR FIRING

The site of the lesion in hemifacial spasm, according to Wartenberg,[16] appears to be the facial nucleus. This author differentiates between 1) "cryptogenic" facial spasm due to infectious or degenerative changes or due to in-

ferior "anlage," 2) "reaction a distance" in lesions of the peripheral branches of the facial nerve, and 3) postparalytic facial spasm following Bell's palsy. Even though this type of hemifacial spasm can be aggravated by emotional stress,[9] we have found that this type of hemifacial spasm can be clearly differentiated by simple electrophysiologic recordings from the psychogenic variety of habit spasms discussed later.

Four of our patients showed evidence of nuclear firing during combined electroencephalographic and electromyographic procedures, subclassified as two cases of cryptogenic facial spasm, one case of "reaction a distance," and one case of postparalytic facial spasm. Contrary to the work of Thiebaut and coworkers,[17] we found no specific way to differentiate the various subtypes of firing electrophysiologically; this seems to indicate a common electrophysiologic mechanism.

Adams and co-workers[20] have pointed out that muscular spasms, including peripheral facial spasms, are "associated with repetitive firing in the motor nerve following one initial excitation . . . . and are associated with repetitive action potentials of the size and duration of those of motor units . . . . in such muscles spontaneous twitching of one or more fasciculi is common during repose." Fasciculation potentials (a term originally used by Denny-Brown and Pennybacker[21] in contradistinction to the smaller and more rapid contractions of single muscle fibers called fibrillations) are seen particularly during repose states after nuclear facial spasms. Since fasciculations repeat at slow rates they can well be recorded by a sensitive inkwriter instrument, unlike fibrillations which require the weightless beam of a cathode ray oscilloscope for adequate recording. We would like to add that fibrillations were also observed by us and others[21] on the cathode ray oscilloscope in the postparalytic type.

A 27 year old white man had a radical left mastoid operation at the age of four. At age 16 he noted twitchings around the muscles of his left eye, which were particularly noticeable when raising his eyebrows on the left (elevation of left frontalis muscle). When examined the twitchings of the left orbicularis oculi muscle were noted to spread also to all the other mimetic muscles on the left as well as to the left auriculotemporal muscle groups. When the cheeks were puffed very definite associated intrafacial movements, that is, a sudden lid drop, were noted.

Electroencephalograph cup electrodes were applied over standard scalp derivations as well as over various facial muscle points. Monophasic and biphasic spike bursts were observed over the facial muscles firing in unison and attaining a voltage of 200 microvolts over the zygomatic muscle, whereas the maximum twitching observed clinically appeared over the left orbicularis oculi muscle. Occasionally the spikes appeared in single forms, but frequently showed repetitive firing at approximately five spikes in two seconds (figure 2A). When recording with coaxial needles placed in the zygomatic muscle, activity resembling a polyphasic, "giant motor unit" type was noted. Irregularly repeating single spikes were also noted during repose. The left orbicularis oculi muscle showed only a reflection of polyphasic spike bursts of very low voltage and no reflection of single spikes as seen in the zygomatic muscle (figure 2B). These single spikes occurred about one to three times per second. The right zygomatic muscle showed a slight "spread" of similar activity of much lower voltage.

Similar activity could be demonstrated in other patients with simple electroencephalogram cup electrodes applied over standard scalp application points and facial muscles.

Figure 3A demonstrates single and double spikes over the left frontal, auriculotemporal, and zygomatic electrode applications, whereas figure 3B shows coaxial needle recordings of the left frontalis muscle demonstrating single

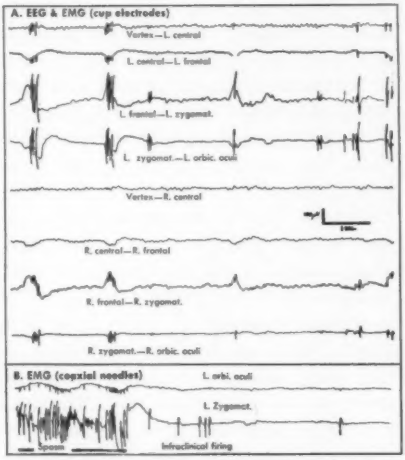

FIG. 2. Hemifacial spasm due to nuclear firing in a 27 year old man. *A.* Repetitive mono- and biphasic spike bursts noted particularly over left zygomatic electrode (heavy line). *B.* Minimal reflection of polyphasic spike bursts and no reflection of single spikes of orbicularis oculi muscle (spikes originating from zygomatic muscle).

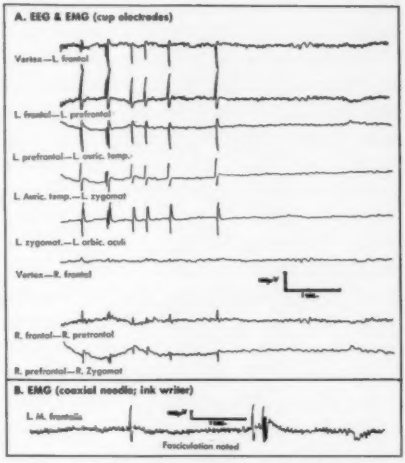

FIG. 3. Hemifacial spasm due to nuclear firing in a 51 year old man. *A.* Single and double spikes derived from left frontal, auriculotemporal, and zygomatic muscles. *B.* Fasciculation potentials recorded with coaxial needles from left frontalis muscle.

and triple spikes. This patient had cryptogenic facial spasms, as did another patient who had maximal spike discharges over the left frontal electrode applications (figure 4A), the recording over the left zygomatic muscle being of much lower voltage. Coaxial needle recordings from the left frontalis muscle obtained during infraclinical firing showed definite single, double, and triple biphasic spikes occurring at irregular intervals (figure 4B).

Neurologic findings: Besides the history of seventh nerve trauma or of preceding facial palsy, "associated movements" were frequently observed in patients with hemifacial spasms; for example, puffing the cheeks produced closure of the left eye. It was also observed that the oculoauricular associated movements as outlined by Wartenberg[16] are usually positive in patients showing "nuclear" firing over the seventh nerve distribution. Facial twitchings persist following sodium Amytal injections or

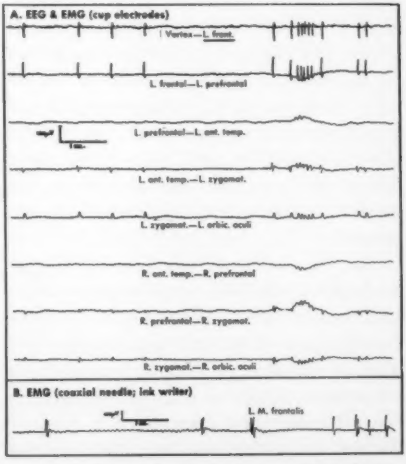

FIG. 4. Hemifacial spasm due to nuclear firing in a 62 year old man. *A.* Maximal single spikes recorded from left frontalis muscle. *B.* Single, double, and triple biphasic spikes occurring at regular intervals (left frontalis muscle, coaxial needle recording).

hypnosis, though sometimes in an attenuated fashion.

Treatment. It is difficult, indeed, to postulate a specific therapy for hemifacial spasms of nuclear origin, particularly since both the postparalytic and cryptogenic facial spasms are refractory to almost any palliative treatment. Many different forms of therapy have been tried. The number and variety of the treatments recommended seem to bear mute testimony to their relative inadequacy. Various attempts have been made upon the integrity or continuity of the facial nerve in an effort to relieve the patient. These attempts range from freezing, novocaine and/or alcohol injections, and stretching of the facial nerve to section and anastomosis of the nerve. Wartenberg[16] stated that only when the executor of the spasm (the facial nerve itself) is eliminated is the patient free of his spasm. Recognizing that no palliative improvement can be expected except by direct attack upon the facial nerve, the mode of treatment followed by the authors for this condition is that of a selective partial neurectomy of the facial nerve. This procedure differs from others in that some of the seventh nerve fibers are sectioned differentially in the predominantly affected divisions of this nerve.

The patient is prepared for a left preauricular operation, usually under Pentothal anesthesia with the patient intubated, to afford a clear vision of the face after the operative site is reached. A curvilinear incision is made bordering the ear, swinging beneath the lobe of the ear and extending downward on the neck for a short distance (figure 5). The approximate location of the nerve within the gland is determined by stimulation studies and the gland is incised, usually near its anterior edge. The dissection is carefully carried down to the trunk of the facial nerve, which is then exposed in its major divisions. Attention is then directed to those branches supplying the area most severely involved. Using the dissecting needles the nerve fibers are teased free of the epineurium (figure 6). One such fiber is then isolated over the needle point and the stimulator applied. If the locus of the response is correct, this fiber is then divided. This attack is continued until enough fibers have been divided in a specific nerve division so that only a limited response in the innervated musculature results. This procedure is followed through those divisions supplying the areas most directly involved. Upon completing this differential section the entire nerve is stimulated to determine the over-all response. The total response will, of course, be considerably less using the same current which had been used to stimulate the nerve at the beginning of the operation. Upon awakening the patient has some weakness when smiling, although some movement of the operative side is noted. Eye blinking, while possible, is somewhat sluggish. There may be some additional paresis which occurs after the third or fourth postoperative day, but this clears subsequently. The end result is that the resting face shows no evidence of paresis on the treated side and shows only slight paresis upon smiling broadly. Eye blinking motions are very nearly normal. Occasional flicker-like spasms are still detectable, although they are not at all disturbing to the patient.

The authors believe that this differential neurectomy, whereby the greater number of fibers to a more severely affected part are divided, is an improve-

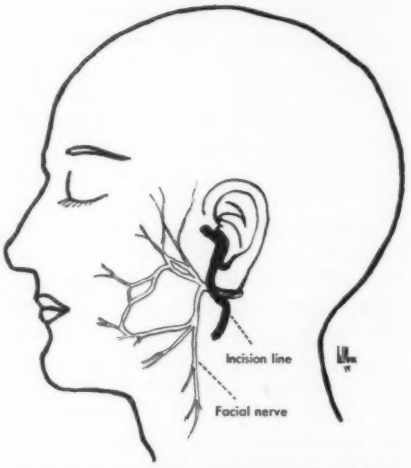

FIG. 5. Placement of incision for selective partial neurectomy of the facial nerve.

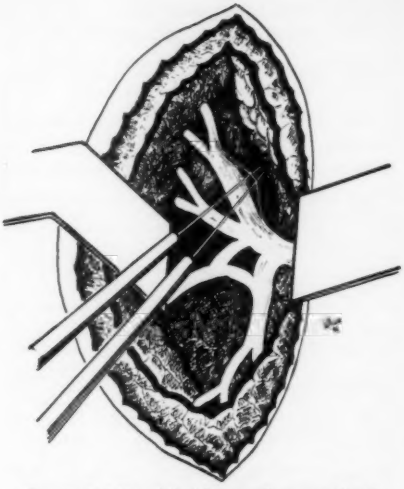

FIG. 6. Isolation of facial nerve fiber over dissecting needles preparatory to stimulation and section.

ment over the previously employed less selective methods of interfering with the executor of the spasm, the facial nerve itself. It is more satisfactory, not only in its functional but also in its esthetic result, considering again that no better specific therapy is known.

Comment. Hemifacial spasms of nuclear origin show a characteristic electromyographic pattern even when recorded with an inkwriter instrument. Characteristic spike firing was noted in an apparently resting muscle. The site of greatest clinical disturbance observed did not always correspond with the site of maximal electromyographic disturbance. This fact was clinically useful when the selective partial neurectomy of the facial nerve was considered as the treatment of choice. No definite electroencephalographic disturbance of cerebral-neuronal rhythmicity was noted when studied with standard surface electrodes.

HEMIFACIAL SPASMS DUE TO PSYCHOGENIC CONVERSION REACTION

Wartenberg[16] stated that the facial "tic is a voluntary, purposive, mimic movement that has degenerated into a habit." In our experience the origin of hemifacial spasms is much more frequently subconscious than conscious and frequently cannot be inhibited by voluntary suppression. Ehni and Woltman[9] stated that hemifacial spasms can be easily differentiated "from other twitching disturbances of the face." It is our experience that these habit spasms often require more than clinical observation for adequate classification. Combined electroencephalographic and electromyographic observations have proved to be a definite diagnostic help in eight patients observed.

A 51 year old white man originally developed eyelid spasms associated with vernal conjunctivitis. At the same time his brother, to whom he was closely attached emotionally, became critically ill and died shortly thereafter.

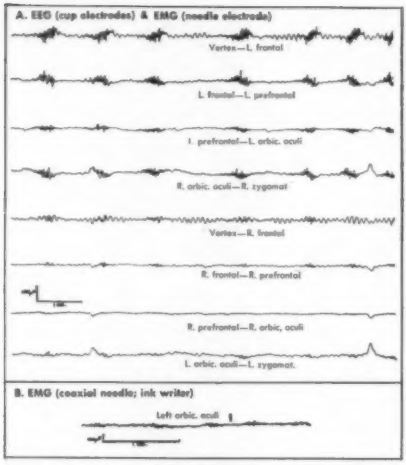

FIG. 7. Psychogenic habit spasm in a 51 year old man. *A*. Rhythmic muscle contraction bursts over all left facial electrode applications. *B*. No single spikes noted as evidences in nuclear firing (compare with figures 2, 3, and 4).

The patient's eyes closed at the funeral and his left eyelid and face began to twitch subsequently. Eventually and characteristically, the right side of his face also became involved, with twitching and spasms over either or both sides. A combined electroencephalogram and electromyogram showed synchronous muscle contraction bursts over all left facial electrode applications, each burst lasting from three to five seconds and showing 10 to 15 rapid muscle spindles per 0.2 second intervals of only 40 to 75 microvolt amplitude (figure 7). No electroencephalographic abnormalities were noted, nor were any high voltage single, double, or triple spikes observed during repose. Characteristically sodium Amytal abolished this tic completely.

Comment. Facial tics are habit spasms due to psychophysiologic conversion reactions. They were noted twice as frequently as hemifacial spasms due to organic etiology. As Herz and Putnam[22] have pointed out, habit spasms frequently affect both sides of the face. Combined electroencephalographic and electromyographic recordings reveal no definite abnormalities except for muscle contraction bursts identical to those seen in voluntary movements. Habit spasms respond occasionally to various psychotherapeutic approaches and can be abolished at least temporarily by intravenous sodium Amytal injections.

SUMMARY AND CONCLUSIONS

1. Hemifacial spasms may be observed in a variety of neurologic disorders, but are then accompanied by additional neurologic signs and symptoms of systemic or regional origin.

2. Hemifacial spasms occurring as isolated neurologic or psychologic phenomena can be classified by simple clinical and electrophysiologic observations into three main categories: hemifacial spasms due to 1) cortical irritation, 2) involvement of the facial nucleus itself, and 3) psychogenic conversion reactions (habit spasms).

3. Hemifacial spasms due to cortical irritation appear to be uncommon. Additional neurologic symptoms due to involvement of adjacent cortical areas initially accompany the spasms. Electrophysiologic abnormalities include repetitive and single spike firing apparently coming from various mimetic muscles. There are actual disturbances of cerebral-neuronal rhythmicity in the electroencephalogram.

4. Hemifacial spasms of nuclear origin can be subclassified as: 1) cryptogenic facial spasm (infectious, degenerative, inferior "anlage"), 2) "reaction a distance" (lesions of peripheral branches of the facial nerve), and 3) postparalytic (following Bell's palsy). All show characteristic electromyographic patterns even with sensitive inkwriter recording, but no definite electroencephalographic disturbances of cerebral rhythmicity.

Associated intrafacial movements are important from a clinical neurologic viewpoint. The site of greatest clinical disturbance does not always correspond with the site of maximal electromyographic disturbance. This bears a relationship to the selective partial neurectomy of the facial nerve as the neurosurgical treatment of choice.

5. Hemifacial spasms due to psychogenic conversion reactions (habit spasm, facial tic) are twice as common as are hemifacial spasms of organic etiology. They affect one or both sides of the face and can be temporarily abolished by intravenous sodium Amytal injections. Combined electroencephalographic and electromyographic recordings show muscle contraction bursts identical to the ones seen in voluntary movements.

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Surgical Occlusion of Anterior Choroidal Arteries in Parkinsonism

Clinical and Neuropathologic Findings

Robert W. Rand, M.D., W. Jann Brown, M.D and W. Eugene Stern, M.D.

SINCE OCCLUSION of one or both anterior choroidal arteries was introduced for the amelioration of parkinsonism by Cooper,[1,2] various investigators have explored the effects of occluding this artery in man and in primates. As a result of these investigations, further information has been presented concerning the pattern of arterial circulation of certain of the basal ganglia and their associated and neighboring structures, as well as the neural mechanism which causes alternating rest tremor.

In a previous paper,[3] early results of surgical occlusion of the anterior choroidal artery in four parkinsonian patients were presented. The present report deals with the follow-up clinical and neuropathologic observations on these four patients as well as one additional patient, all five of whom were refractory to medical treatment.

ANALYSIS OF CASES

All five patients were males whose ages varied from 44 to 60 years. Three of them were postencephalitic, a fourth had a history of syphilis, and the fifth had an idiopathic process that dated from 14 years of age.

A typical clinical picture had been present in the postencephalitic patients for five, 24, and 26 years, respectively. Severe rigidity occurred in these three patients, accompanied by a mild to severe alternating tremor in two of them. The other two patients had mild to moderately severe rigidity and a severe alternating tremor of nine and 30 years' duration that was limited to the right side.

In the two patients with unilateral syndromes, the contralateral anterior choroidal arteries were occluded. In the remaining three cases, this artery was occluded on the right side in two instances and bilaterally in one.

SURGICAL FINDINGS

The five patients had six operations, the operative technic employed being similar in all instances. The anterior choroidal arteries were exposed by way of a temporal osteoplastic craniotomy. In four instances these vessels were normal in origin, course, and size; in the fifth, the anterior choroidal artery was

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Presented in part at the neurosurgical section of the fortieth annual clinical congress of the American College of Surgeons, Atlantic City, November 1954.

double from its origin; in the sixth, it was less than a millimeter in diameter. Neither pathologic changes of nor definite anastomoses between, the anterior choroidal artery and adjacent vessels were noted; in the last patient, however, a possible anastomotic vessel arising at the junction of the posterior communicating and internal carotid arteries was occluded. The arteries were clipped in all instances and electrically coagulated in all but the first case. Four to 5 mm. of artery were occluded in the first five operations and 10 mm. in the sixth.

CLINICAL FINDINGS AND RESULTS

Immediate and complete cessation of the alternating tremor occurred on the contralateral side and persisted for a 24-hour period in three of the four patients who suffered this disability. Within two weeks the tremor returned to its preoperative intensity. No change of any kind was observed in the tremor of the fourth case (a small anterior choroidal artery).

In the three postencephalitic cases, the rigidity greatly lessened postoperatively on the side opposite to the arterial occlusion, only to return shortly thereafter; the rigidity in the two patients with unilateral syndromes, however, remains lessened to date. No immediate or delayed postoperative improvement of the other symptoms of parkinsonism, including oculogyric crises, was noted.

A transient, incomplete, left, superior, homonymous quadrantanopsia occurred in the second case, and a thus far permanent, incomplete, left, homonymous hemianopsia in the fifth patient. Significant changes in the pre- and postoperative audiograms and electroencephalograms were not observed. No alterations of blood electrolytes or renal and hepatic function tests were noted, apart from those generally found after a craniotomy.

Two patients have subsequently died. The first patient, in whom the right anterior choroidal artery was occluded, died six weeks postoperatively from tuberculous pneumonia; the second, who had a bilateral anterior choroidal artery obliteration, died of bronchopneumonia ten months after operation. A complete autopsy examination was performed in each case. The details of these two cases are presented and will be emphasized in this communication.

CASE REPORTS

Case 1. A 59 year old right-handed male with postencephalitic parkinsonism of 24 years' duration presented a symptom complex of bilateral, alternating rest tremor, stooped, shuffling gait, masked facies, drooling, and a progressive, almost symmetric rigidity. For the six months prior to surgery he was unable to walk. The age of onset of the disease and the general appearance of the patient suggested an etiologic relationship to a previous subclinical or unrecognized encephalitis.

Examination. The patient was an elderly appearing, thin white male, who sat or lay in bed with his knees and hips slightly flexed, a masklike facial expression, a constantly open mouth, and fluttering eyelids. He was well oriented, alert, and cooperative, and probably of average intelligence. The patient's head was scaphoid; the visual fields were normal. A slight, rhythmic tremor of the tongue was noted during movement but not at rest. Facial movements were difficult. The patient spoke in monosyllables with great difficulty. Although he fatigued quickly and his muscular activity was generally weak, examination of the trunk and extremity musculature disclosed no paresis of any specific muscle groups. Arthritis and rigidity, however, prevented his walking.

Moderately severe, generalized muscular rigidity and cogwheel phenomenon were noted in all extremities. The deep tendon reflexes were more active on the right, and the plantar response was abnormal on the left.

The alternating rest tremor (of a rate of

4 to 6 per second) stopped completely during voluntary movement. It involved the upper extremities about equally and was particularly evident in the hands, producing the "pill-rolling" effect. Occasional tremor was observed in the lower extremities and may have been related to the internal rotation and plantar flexion of the feet, which were fixed deformities.

Laboratory data. Studies of the blood, urine, and cerebrospinal fluid were normal. These included blood chemistry studies, serologic tests, and renal and hepatic function tests. Roentgenograms demonstrated thickening of the skull table and a mild degree of platybasia. Electroencephalograms, awake and asleep, were normal.

Operation. On November 24, 1953, under general anesthesia, the right anterior choroidal artery was found to arise from the posterior surface of the internal carotid artery about 5 mm. above the posterior communicating artery. The vessel was clipped near its origin and again 4 mm. along its course (figure 1). Electrocoagulation was not used. Vital signs were unchanged following occlusion.

Hospital course. During recovery from anesthesia and shortly thereafter, there were no abnormal movements on the left side. During the first 24 hours, however, some episodes of alternating tremor on the left appeared and soon became constant. For the first three days the rate of tremor seemed unchanged, but the severity was strikingly reduced even during periods of severe emotional disturbance. From the fourteenth day the tremor on the left was generally 20 to 25 per cent less than on the right; at times, the difference was even more striking; at other times, the two sides were indistinguishable. Except for this change in tremor, the neurologic findings remained the same. Following onset of the terminal illness six weeks postoperatively, the tremor gradually increased and finally was as severe and constant as it had been preoperatively. The patient died on the forty-second postoperative day from tuberculous pneumonia.

Postmortem examination. Both lungs were heavy and filled with fluid. The lower lobes showed bilaterally an extensive, tuberculous pneumonitis which was manifested by exudate, small cysts, and scarring, admixed with yellow caseous nodules.

Gross description of the central nervous system. The brain with cerebellum and brainstem attached weighed 1,600 gm. The leptomeninges were thin and transparent. The cerebral hemispheres were symmetric and showed no gross abnormality, except a slight widening of the sulci. There was mild molding of the cerebellar tonsils about the medulla, and several small, superficial foci of traumatic encephalomalacia were present in the right inferior temporal gyrus, just lateral to the uncus. The vessels of the circle of Willis revealed no atherosclerotic plaques but were somewhat milky and fibrotic in appearance. There was a silver clip across the right anterior choroidal artery approximately 4 mm. distal to its origin from the internal carotid artery. Proximal to the clip, the lumen of the vessel was filled with a red-blue thrombus, which proved to be partially organized.

The coronal sections revealed normal basal ganglia; there was some widening of the perivascular spaces in the putamen. Infarctions were not noted in the basal ganglia, hippocampi, optic tracts, or lateral geniculate bodies. The substantia nigra and locus caeruleus were extraordinarily pale. Sections through the cerebellum and brainstem revealed no abnormalities.

Microscopic description of the central nervous system. The diencephalon, mesencephalon, and upper pons were serially sectioned at 60 to 120 microns and studied in hematoxylin and eosin and Weil preparations. There was no focus of demyelination. The neurons of the substantia nigra were almost completely absent. The few remaining nerve cells showed loss of pigment and a rare pink, round hyalinized mass in the cytoplasm. There was some scattered melanin pigment near small blood vessels. The glial fibers and neuroglial cells occupied a major portion of this nucleus.

Case 2. A 46 year old, right-handed white male developed encephalitis at the age of 15 during an attack of influenza. Five years later stiffness and weakness in his legs ensued. Subsequently the rigidity increased, appeared in the upper extremities, and fused into a typical parkinsonian syndrome which produced oculogyric crises, masked facies, difficulty in deglutition and phonation, and some alternating rest tremor of both feet. The patient could barely walk.

Examination. The patient was thin, his shoulders were stooped, and his deformed feet were

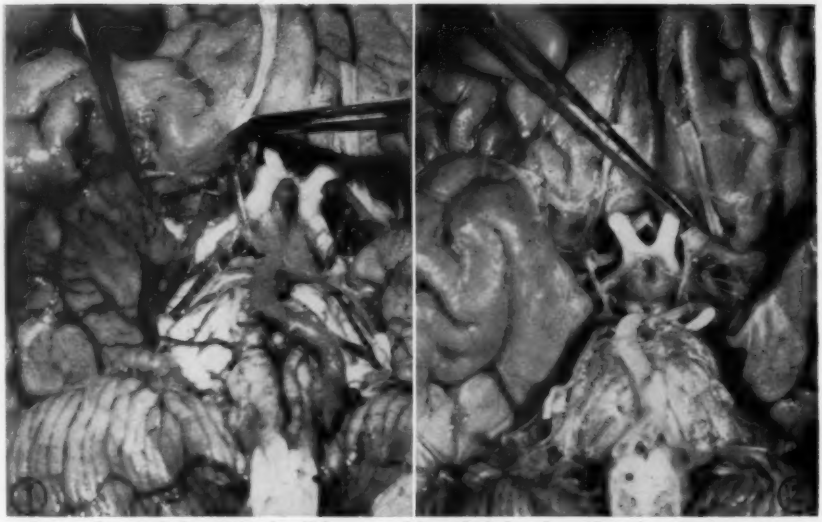


FIG. 1. *Case 1.* Right anterior choroidal artery and its multiple branches with a silver clip (arrow) approximately 4 to 5 mm. from its origin. Note dark thrombus formation in proximal segment.
FIG. 2. *Case 2.* Right anterior choroidal artery occluded for 4 to 5 mm. by silver clips and fulguration.

inverted. He was mentally alert and oriented but spoke with a slow, explosive voice. Visual fields were generally constricted. Episodes of oculogyric crises resulted in an uncontrolled turning of the eyes upward and to the right. Deglutition was difficult and the tongue showed a coarse, rhythmic tremor. There was a severe, generalized rigidity of the trunk and extremities, but the arms were more involved than the legs. The cogwheel phenomenon was present throughout. Although weakness was general, there was no specific paresis. A rhythmic, alternating rest tremor (of 4 to 5 per second) involved both feet; less tremor was noted in the hand. The superficial abdominal reflexes were absent on the left; the deep tendon reflexes were greater on the left. If assisted, the patient could walk with short, shuffling steps.

Laboratory studies. Except for a cerebrospinal fluid protein of 90 mg. per cent, laboratory studies showed no abnormalities. Roentgenograms of the skull were normal. Electroencephalograms, awake and asleep, were normal. An electromyogram revealed a tremor of 4 to 6 per second in the lower extremities.

Operation. On November 30, 1953 the right anterior choroidal artery was exposed in a manner similar to that of the first case. The visualized arteries were normal in size, course, and appearance. Fine branches arose from the anterior choroidal artery close to its origin from the internal carotid artery. The vessel was occluded over a distance of 5 mm. by two silver clips, and the coagulation current was applied to the second clip so that the segment of artery between the clips and slightly beyond was darkened and obliterated (figure 2). The vital signs remained unchanged during this procedure.

Postoperative course. The tremor in the lower extremities disappeared for 24 hours, but was noted bilaterally on the second postoperative day, and assumed its former intensity by the end of the first week. The degree of rigidity, however, decreased to one-half of its intensity in the left lower extremity; there was a subtle decrease in the upper extremity. By the tenth day the initial improvement had stopped, and the other manifestations of the disease seemed slightly worse than before operation.

During the third week it was difficult to discern any significant difference between the rigidity on the left and right sides, but by the

end of the fourth week the patient was able to make voluntary movements more easily with his right arm than with his left. This status continued up to the time of the second operation.

On several occasions visual field examinations had shown the presence of a partial left superior quadrantanopsia; no other neurologic changes appeared.

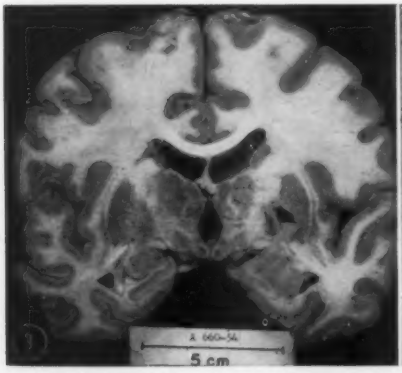
Second operation. On January 12, 1954 the left anterior choroidal artery was exposed. It arose as a double vessel from the posterolateral aspect of the internal carotid artery about 5 mm. superior to the posterior communicating artery. The first silver clip enclosed both branches; a second clip was placed about 2 mm. distally on the larger artery. Approximately 5 mm. of these vessels were desiccated with the coagulating current.

Postoperative course following second operation. All tremor in the lower extremities ceased initially, but gradually returned in the left lower extremity and to some degree in the hand. Resistance to passive movements of all extremities was greatly reduced. This was particularly true of the right arm, but slowly the rigidity returned to all extremities and became more severe on the left side than it had been prior to the first surgical procedure.

Despite continued physiotherapy and early wheel-chair ambulation, this patient's condition worsened and he died during an episode of bronchopneumonia ten months after the first surgical procedure.

Postmortem examination. At postmortem examination the body was extremely emaciated. The lungs revealed a bilateral, diffuse, severe bronchopneumonia, characterized by a granular-appearing cut-surface, nodularity, and consolidation. The organism was not identified.

Gross description of the central nervous system. The leptomeninges were thin and transparent. The brain weighed 1,600 gm. The cerebral hemispheres were symmetric with a normal gyral pattern but with some widening of the frontal lobe sulci. The vessels of the circle of Willis were thin and delicate and contained no atheromatous plaques. Two silver clips were attached to the left anterior choroidal artery, approximately 1 and 4 mm. distal to the internal carotid artery. Beyond the latter clip, the artery was brown and friable from fulguration. The right anterior choroidal artery was similarly occluded. Sections of these arteries revealed fibroblastic proliferation and obliteration of the lumens. The cerebrum was sectioned coronally. At the level of the mammillary bodies on the left, there was an area of cystic malacia which extended completely across the internal segment of the globus pallidus (figures 3, 5, and 7). The cyst was pigmented a light tan color, measured 1 x 0.4 cm., and was bounded by the optic tract and amygdaloid nucleus inferiorly and the internal cap-



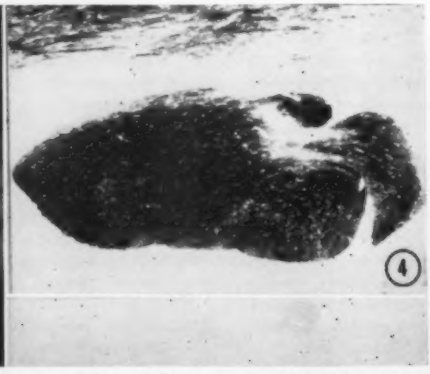


FIG. 3. *Case 2.* Coronal section demonstrating infarction of the medial segment of the left globus pallidus. Note sharp cleavage plane between lateral and medial segments. No gross infarction was seen in right basal ganglia.

FIG. 4. Microphotograph of coronal section of left optic tract showing demyelination in its superior portion. Weil stain.

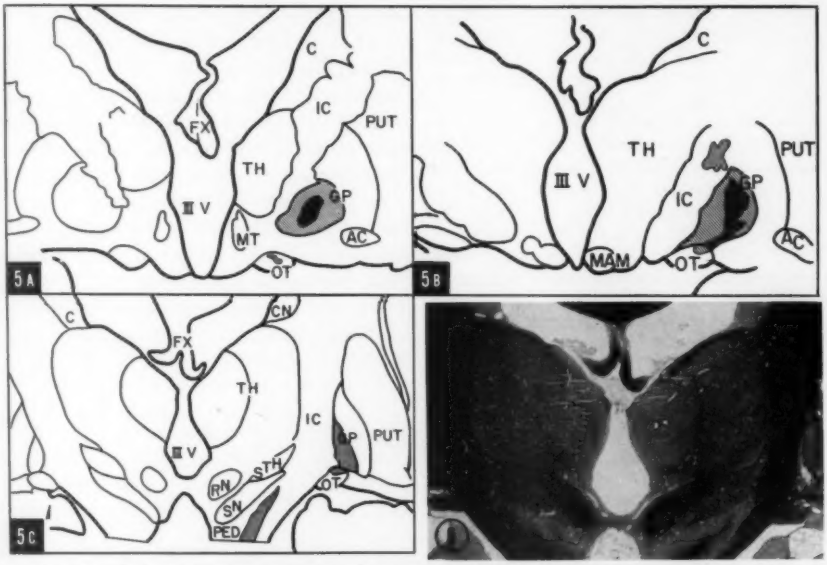


FIG. 5. *A, B, C.* Schematic representation of areas of demyelination and nuclear loss in various levels of the diencephalon.

FIG. 6. Microphotograph of coronal section of thalamus and basal ganglia demonstrating cystic malacia of the medial portion of the left globus pallidus with demyelination of ansa lenticularis, fasciculus lenticularis, fasciculus thalamicus, cerebral peduncle, and optic tract. Weil stain.

sule medially. The perivascular spaces were widened in the white matter of the temporal lobe. The globus pallidus on the right showed no gross abnormalities, and the lateral geniculate bodies and hippocampi appeared normal. The substantia nigra was very pale. Further sections throughout the brainstem and cerebellum were not remarkable.

Microscopic description of the central nervous system. The sections of the diencephalon and mesencephalon (60 to 120 microns) were studied in hematoxylin and eosin and Weil preparations. The superior portion of the optic tract on the left at the level of the anterior thalamus showed a small, irregularly-shaped area of demyelination (figure 4). In addition to rather definite areas of myelin loss in the optic tract, scattered myelin sheaths showed fusiform and balloon-shaped swellings and irregularities. Occasional gitter cells and lymphocytes were seen.

In the medial tip of the inner segment of the globus pallidus on the left side, there were innumerable small cystic spaces which contained gitter cells. The fibers of the internal capsule appeared normally outlined, but the fibers entering from the globus pallidus could be traced for quite a distance because of swelling and bizarre outlines in the sheaths. There were no abnormalities noted in the hypothalamic nuclei.

The optic tract on the right side was normal. The globus pallidus on the right, however, showed focal and diffuse demyelination of the sheaths that entered the internal capsule. There was a thin, linear cystic area in the extreme periphery of the right putamen immediately beneath the internal capsule. Numerous gitter cells were seen in the edges of this cyst, which extended the entire length of the putamen (figure 7).

The cystic spaces in the inner segment of the globus pallidus on the left involved the entire nucleus posteriorly. The diffuse demyelination in the globus pallidus, ansa lenticularis, and fasciculus lenticularis at the level of the

mammillary bodies coalesced with the lesion in the superior quadrant of the optic tract (figures 5 A, B, and C, 6, and 7). At this point a sharply outlined lesion began to appear in the internal capsule. The focus of demyelination in the left optic tract and inner segment of the globus pallidus continued posteriorly throughout the course of the tract and extent of the nucleus. Ultimately, the demyelinating lesion in the left internal capsule was seen in the left peduncle, as well as in the ansa lenticularis, fasciculus lenticularis, and fasciculus thalamicus. As judged by the astrocyte and gitter cell response, all the lesions noted appeared to be of approximately the same age. In the hippocampal gyrus on the left, there were foci of neuron loss and increased numbers of neuroglial cells.

DISCUSSION

The pathophysiology of parkinsonism, particularly the rest tremor, remains an enigma which has provoked many theoretical explanations. Some students of this problem visualize the origin of the tremor as arising primarily in the uninhibited cerebral motor cortex and associated pyramidal tract.[4] Others, including Cooper,[5] have speculated that abnormal discharges resulting in tremor arise from the diseased pallidum. Magoun[6] and Jenkner and Ward[7] regarded the reticular substances of the mesencepha-

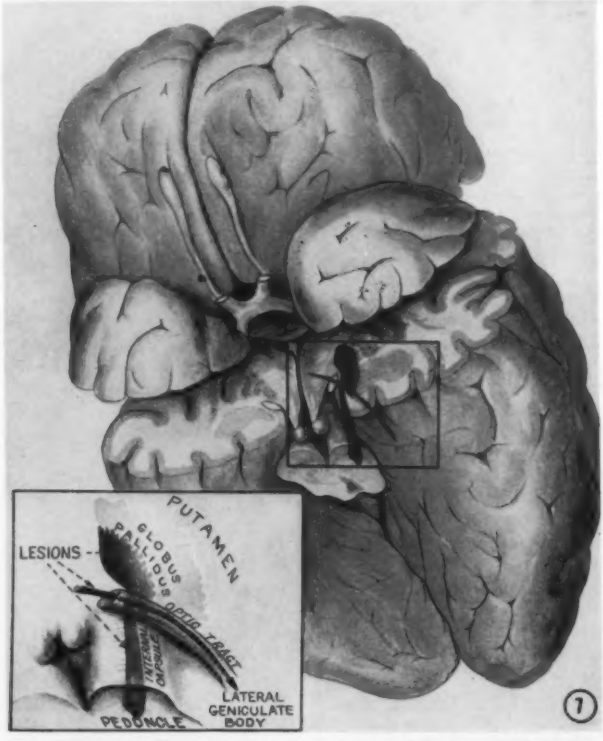


FIG. 7. Schematically composed drawing of areas of involvement. Note thin cystic area in right putamen.

lon and pons as the tremorgenic area which is released by lesions in more cephalad structures. Spiegel and Wycis[8] have concluded from their studies of patients undergoing ansotomy "that at least part of the pallidofugal impulses has a facilitating effect upon the tremorgenic area of the reticular substance."

Browder and Kaplan[9] believe that the basal ganglia area and its associated pathways supplied by the anterior choroidal artery are concerned with an abnormal hypothetical circuit or pathway, and that sublethal injury of its cellular elements by anoxia or hypoxia results in a slowing frequency of their firing.

We were impressed by the completeness, even though temporary, of the cessation of tremor in three of four cases and the concomitant or independent amelioration of rigidity in all five of our cases. Although temporary in the severe cases, improvement persisted in the instances where rigidity had been mild. Since paresis of the contralateral extremity did not occur in the cases which did show some improvement, support is given to those who believe[5,10] that the intact pyramidal tract is not the tremor-conducting pathway, but rather that the extrapyramidal circuits are involved. From our present material it would seem reasonable to state that ischemia of the pallidum and the neighboring basal ganglia and their efferent systems resulted in an interruption of the tremorgenic and/or the rigidogenic neural circuits or one of their facilitatory circuits, thus bringing about temporary cessation of tremor and amelioration of rigidity in certain instances. This blockage was not permanent, either because the damage was not of sufficient degree and extent, or because other uninvolved neural circuits assumed or continued the task of producing the tremor and rigidity or of facilitating their production.

ANATOMIC DATA: THE ANTERIOR CHOROIDAL ARTERY

Carpenter, Noback, and Moss[11] studied the anatomic aspects of the anterior choroidal artery in 60 cerebral hemispheres and reviewed the pertinent literature summarizing the studies of Duret, Heubner, Kolisko, Beevor, Abbie, and Alexander. As the result of these various investigations on the origin, course, and anastomoses of this artery, it is now generally agreed that the principal branches of the anterior choroidal artery distribute blood to the globus pallidus, the uncal areas of the temporal lobes, the midportion of the cerebral peduncle, the optic tracts and their associated lateral geniculate bodies, the posterior portion of the internal capsule, and, in part, the auditory radiations before supplying the choroid plexus. Carpenter and co-workers emphasized the occasional origin of the anterior choroidal artery from the middle cerebral artery, the posterior communicating artery, and the junction of the middle and anterior cerebral arteries. Various anastomoses between the anterior choroidal artery and closely neighboring vessels have been recognized by Kaplan[12] and Godinov.[13] Variation in the territory irrigated by this vessel also has been noted by Alexander.[14]

PATHOLOGIC CONSIDERATION FOLLOWING ARTERIAL OCCLUSIONS

Until the advent of surgical occlusion of the anterior choroidal artery for parkinsonism, the significance of possible anastomotic connections had not been fully appreciated. Examination of the brain in case 1 demonstrated that, de-

spite occlusion of the first 4 mm. of the right anterior choroidal artery (figure 1), no gross or microscopic areas of necrosis were present in the area of supply. The only reasonable explanation for the lack of infarction was that the blood was flowing through various possible anastomoses which had not been evident at operation. We confirmed the patency of such anastomoses by injection studies.

Although Alexander[14] pointed up the vulnerability of the anterior choroidal artery to thrombosis, the pathologic studies in our series demonstrate that degenerative and anoxic changes in the structures supposedly supplied by this artery do not consistently occur in the presence of proved thrombosis of the first 4 to 5 mm. of this vessel. If infarction does occur, the globus pallidus and closely associated structures may be affected. It is noteworthy that proved infarction of the globus pallidus and adjacent structures occurred only once following acute occlusion of three anterior choroidal arteries (figure 6). If a major cerebral artery is occluded, it is highly probable that the lower the systemic blood pressure, the greater will be the area of brain damage.[15,16] In our series of cases it is conceivable that, if hypotension had been induced,[15] additional necrosis and infarction might have occurred following acute occlusion of the anterior choroidal artery.

Pathologic studies by Mettler and coworkers[17] of similar examples of surgical occlusion of the anterior choroidal arteries underscore the marked variability of resulting brain damage. After studying the effect of anterior choroidal artery occlusion in the chimpanzee, they theorized that, to account for the failure or the varied pattern of infarction, either anastomoses between the anterior choroidal artery and the posterior communicating artery or a high degree of overlap of their branches must exist.

In our material (case 2) and apparently in other human cases alluded to by Mettler and co-workers[17] and Kaplan,[18] the medial segments of the pallidum were also necrosed. Sparing of the lateral segment of the globus pallidus in the presence of infarction of the inner segments may be explained on the basis that its arterial supply is frequently made by striate vessels. The infarction which occurred along the periphery of the putamen in case 2 rather than at the junction of the medial and lateral segments of the globus pallidus or the globus pallidus and putamen suggests that, in certain instances, the putamen may also be partially supplied by the anterior choroidal artery.

SURGICAL CONSIDERATIONS

Morello and Cooper[20] pointed out that the anterior choroidal artery can be demonstrated in about 92 per cent of satisfactory cerebral arteriograms, and that the lack of filling postoperatively would be strong supportive evidence of occlusion. Because the tremor in one of our cases of unilateral parkinsonism remained unchanged and only transient improvement occurred in the second similar case, postoperative angiography was carried out. These studies failed to reveal filling of the anterior choroidal artery in either instance (figures 8 and 9). In both cases the rigidity was ameliorated and continued to be lessened at the time of this writing. It is significant that in the first of these two patients (figure 8) the anterior choroidal artery was definitely smaller than any we had previously observed, and

FIG. 8 and 9. Cerebral angiograms. Note lack of filling by Diodrast in the left anterior choroidal arteries following their occlusion by clipping and electrocoagulation.

it may well be that the striate branches of the middle cerebral artery and the branches of the posterior communicating artery, along with other neighboring vessels, are directly supplying the regions generally irrigated by the anterior choroidal artery.[11,14]

In view of the occurrence of early branching of the anterior choroidal artery,[11] Cooper[19] advocated electrocoagulation of 1 cm. of the anterior choroidal artery. He has also occluded the posterior communicating artery in some cases, apparently to insure infarction of the pallidum.[21] Such electrocoagulation of 1 cm. of the anterior choroidal artery was carried out in our fifth patient without improvement; in fact, a persistent mild hemiparesis, hypesthesia, and homonymous hemianopsia contralateral to the side of occlusion resulted.

Case 2 emphasizes the fact that, at least in cases where rigidity is the major symptom, the parkinsonian syndrome may be unchanged in the presence of infarction of the supposedly desired structures. The postoperative neurologic picture of our fifth patient who had rigidity as a preoperative symptom would indicate that necrosis had occurred in the optic tract, and/or lateral geniculate body, and in the internal capsule; thus, it probably involved the globus pallidus and efferent systems. This patient showed no improvement.

That involvement of the corticospinal pathways may be more extensive than in the case reported here is indicated by the following additional experience: One of us occluded the right anterior choroidal artery in a young man who had severe generalized parkinsonian rigidity and tremor of ten years' duration. The vessel was clipped and fulgurated over a distance of 1 cm., together with an anastomotic branch between the posterior communicating and anterior choroidal arteries. The procedure went smoothly and other vessels and structures were not disturbed. Upon recovery from anesthesia, a profound, semipermanent, left hemiparesis was present. With the resolution of weakness, the tremor has returned.

RESULTS OF OCCLUSION

Doshay[22] summarized his observations of four patients and concluded that the operation has proved beneficial for selected young postencephalitic patients but is of limited value otherwise. Pool[23] communicated that in six cases of parkinsonism (including the four noted by Doshay) only temporary improvement was obtained, and he believes that the procedure is satisfactory only in rare cases. Cooper's more recent publication[5] is more hopeful, but represents the only such encouraging report.

In summary, our personal experience is this: Tremor was only temporarily abolished or reduced in three of four patients; mild rigidity was abolished in two and partially relieved in one of five patients so afflicted. The production of an infarct in the desired area is capricious, and even in the presence of a hoped-for infarction the tremor and rigidity may not alter sufficiently to consider the end result satisfactory.

From our anatomic, clinical, and pathologic studies we have found that several factors determine the production of an infarct in the regions supplied by the anterior choroidal artery after its surgical occlusion: 1) the distribution of the artery and the site or origin of the major branches; 2) the size of the artery; 3) the number of functional anastomoses in the subarachnoid space between neighboring arteries and the anterior choroidal artery and, perhaps, the presence or absence of precapillary and capillary anastomoses with neighboring intracerebral arteries; 4) the presence of disease processes involving the cerebral arteries, particularly the anterior choroidal artery and its branches; and 5) the status of the cerebral hemodynamics at the time of arterial occlusion and during the early postoperative period.

Thus, we believe that the cause of our disappointing clinical results following occlusion of the anterior choroidal artery for parkinsonism was failure to produce appropriate lesions. Variable circulatory factors and apparent "recircuiting" of the tremorgenic and rigidogenic neural impulses and/or their facilitatory impulses preserved the imbalance created by the disease process.

SUMMARY

An analysis of the treatment of parkinsonism by surgical occlusion of the anterior choroidal artery is presented with case documentation and a review of the pertinent literature. The detailed pathologic examinations made of four hemispheres following anterior choroidal artery occlusion are presented. The distribution of the lesions, when present, varied both in location and extent within the areas supposedly supplied by this artery. The failure to alleviate the symptoms of parkinsonism and the attendant complication of paresis was disappointing. The reasons for failure are discussed.

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■ Clinical observation teaches, as I have already shown, that an alteration of a lateral half of the pons Varolii or of the medulla oblongata, above the decussation of the anterior pyramids, causes a paralysis of voluntary movements in the opposite side of the body, and not at all in the corresponding side. This fact, assuredly, proves that the decussation of the fibres employed in voluntary movements takes place entirely below the place altered, because if the decussation were not achieved below this place, there would be some degree of paralysis in the side of the body corresponding to the side altered in the basis of the encephalon – which is not the case – and the paralysis in the opposite side would not be complete, which also is not the case. From these facts we could, therefore, conclude already, that the anterior columns of the spinal cord near the medulla oblongata are not the channels for the orders of the will to muscles, as anatomy shows that these columns do not decussate in the lower part of the medulla oblongata. It might be said, however, that these columns, perhaps, make their decussation in the spinal cord itself; but this hypothesis is disproved by many pathological cases, showing that an alteration of a lateral half of the spinal cord causes a loss of voluntary movements only in the corresponding side.

C. E. Brown-Séquard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

Vascular Phenomena Involving Brainstem Structures

A Clinical and Pathologic Correlation Study

Harry C. H. Fang, M.D. and J. J. Palmer, M.D.

THE GROWING CONCERN with cerebrovascular disease during recent years has not been without reason. The advent of antibiotics and other advances have increased life expectancy to a certain degree. Yet the problems of aging and of the degenerative diseases which are common to advanced age have been similarly increased. From the standpoint of cerebrovascular disease, the latest figures available on incidence are quoted by Wright[1] as follows:

1. In 1952, 170,000 people died in the United States of cerebrovascular accidents.

2. The estimated number of victims of cerebrovascular disease in the United States is 1,800,000.

3. Cerebral arteriosclerosis is the second leading cause of first admissions to the state mental hospitals, schizophrenia being the leading cause.

4. Seventy-three per cent of deaths caused by cerebrovascular diseases in 1952 occurred in people 65 years of age or older.

Kubik and Adams,[2] Denny-Brown,[3,4] Millikan and Siekert,[5,6] Denny-Brown and Foley,[7] and others have presented the various aspects of basilar arterial disease, both from the standpoint of clinicopathologic correlation and of clinical recognition of diverse brainstem vascular states, including those of intermittent circulatory insufficiency. Foix and Hillemand[8] have contributed to our understanding of the blood supply of brainstem structures and have defined two vascular syndromes: 1) paramedian variety, manifested by either hemiplegia or, if bilateral, quadriplegia, and 2) lateral tegmental syndrome, characterized by crossed hemiplegia or crossed sensory loss and ipsilateral asynergy.

In regard to the incidence of basilar artery occlusion in a general hospital, Kubik and Adams[2] reported 25 cases in 7,400 consecutive autopsies, or one case

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This work was supported in part by the U.S.P.H.S.—Grant No. B-265 (C).

Presented in part at the seventh annual meeting of the American Academy of Neurology, Houston, Texas, April 29, 1955.

TABLE 1

Total Number of Autopsies in two years		1,687
Cerebral arteriosclerosis		295
Brain softening		200
Thrombosis of cerebral artery identified		
Carotid system		31
Basivertebral system		23
Brain hemorrhage		56
Cerebral	34	
Cerebellar	5	
Brainstem	17	
Primary hypertensive pontine hemorrhage	5	
Secondary brainstem hemorrhage	12	
Cerebral embolism		3
Spontaneous subarachnoid hemorrhage		18
Aneurysmal rupture		7

in every 300 general autopsies. At the Mayo Clinic Siekert and Millikan[9] found one case in every 450 autopsies (in adults) in the last five years. We have found eight verified cases of basilar artery occlusion in 1,687 consecutive autopsies, or one in every 210. This higher incidence in our material may be due, in part, to a relatively older age group in our patient population. The mean age for patients hospitalized at Veterans Administration Center, Los Angeles, during the fiscal year of 1953-1954 was 49.02 years.

Recently Wright,[1] Gilbert and de Takats,[10] Millikan and Siekert,[6] and others have stimulated renewed interest in this field of cerebrovascular disease through their recommendation of active therapy. The major aim of this study is to amplify the protean nature of the clinical manifestations of basilar arterial disease, and to emphasize that such disease – be it occlusive, aneurysmal (with or without rupture), or functional insufficiency – occurs with such frequency as to warrant special attention.

CASE MATERIAL

Our material is drawn from the Los Angeles Veterans Administration Medical Center, both from the autopsy files of the department of pathology and the clinical records of the neurology section. A detailed survey covering the two year period between January 1953 and January 1955 was made. Out of 1,687 consecutive autopsies performed during this period, 200 cases of brain softening were found with or without thrombotic occlusion of a major cerebral artery. Infarction necrosis of varying degree of age and intensity was found in the brainstem in 56 instances (28 per cent) (tables 1 and 2). Of the cases of brain softening with verified major arterial occlusion, eight involved the basilar artery. We have reviewed the clinical records and autopsy protocols of 50 cases of cerebrovascular disease involving brainstem structures. Out of this group we have selected 17 cases that may be conveniently grouped in the following way:

1. *Verified cases*
   - *a.* Basilar artery occlusion–7 cases.
   - *b.* Basilar artery aneurysm–3 cases (one of which overlaps with case 2 of group *a*; case 8 was verified at necropsy, case 9 by vertebral angiography).
2. *Nonverified cases*
   - *c.* Basilar artery syndrome (or the intermittent insufficiency states of the basilar artery)–8 cases. Diagnosis was made in every instance on clinical grounds only.

VERIFIED CASES

a. Basilar artery occlusion. This group comprises seven cases of confirmed thrombotic occlusion of the main trunk of the basilar artery. Age distribution was from the fourth to the

TABLE 2

	Cases	*Per Cent*
Brain softening with or without thrombotic occlusion demonstrated	200	
Brainstem softening	56	28.0
Pontine softening	37	18.5
Medullary softening	12	6.0
Midbrain softening	7	3.5

eighth decades, with four of the seven in the seventh decade of life. Duration of survival was from six days to 12 weeks. Preexisting hypertension was found in six of the seven cases. The mode of death was that of respiratory failure of central origin, common to all seven. Four out of seven had diagnosed hypertensive heart disease and one had rheumatic heart disease. Abnormally elevated spinal total proteins were found in three instances, ranging from 77 mg. per cent to 90 mg. per cent.

Case 1. A 41 year old man experienced sudden onset of dizziness, unsteadiness in walking, and forced deviation of the eyes to the right several hours before admission. He was a known hypertensive of 11 years' duration. Five weeks prior to entry he vomited continuously for 24 hours, following which he had periodic headaches. On several occasions he experienced "flickerings" before his eyes. One week later he suddenly could not see the lower half of objects in front of him with either eye. Two weeks before admission he noticed difficulty in maintaining balance while walking and also was noted to be lethargic. Two days earlier his wife noted changes in his speech consisting of slight thickness and stumbling over words. On the day of hospital entry, while talking to his neighbor, he suddenly felt dizzy and staggered, and his eyes seemed to bulge and were forcibly deviated to the right, remaining in this position for five minutes. During the entire episode he was able to converse with his wife. He had at least two episodes of sensation of whirling of the room around him in the counterclockwise direction. He had no previous history of illness except for hospitalization for three weeks in 1950 because of persistent pain in the right supraorbital area and lightheadedness.

At admission examination he was conscious but unable to give an adequate history. Blood pressure was 180/90. Both physical and neurologic examinations were negative. Lumbar puncture revealed clear, colorless fluid with four lymphocytes. Several hours after admission the patient suddenly developed slurred speech, right central facial weakness, staggering gait with tendency to fall to the right, marked cerebellar incoordination involving the right upper limbs, and hyperactive deep tendon reflexes on the right. By the following morning he manifested clonic convulsive movements, with head and eyes turned to the right. He retched, salivated, and perspired profusely, but was conscious and able to grunt answers to questions. Later he became comatose. When seen shortly thereafter, the arms were flaccid and the legs rigidly extended. His vital signs were temperature 100° F., pulse 110, respiration 24, and blood pressure 200/100. He showed ptosis of the left lid and lateral deviation of the right eye. Pupils were unequal in size, the right being slightly larger than the left. There was right central facial weakness. Deep tendon reflexes were hyperactive throughout, with greater preponderance on the right. There were bilateral sustained ankle clonus and bilateral extensor plantar responses. The patient grunted to squeezing the Achilles tendon. Peripheral palsy of the left seventh cranial nerve was found on the following day. He responded to verbal commands of the simplest order, for example, to open and close his eyes. He could also follow an examiner around the room with his eyes. He withdrew arms when the skin was pinched. There were no spontaneous leg movements observed. Bilateral extensor plantar responses were elicited. Two days later he developed flaccid quadriplegia. His course remained static until the eighth week of hospitalization when his rectal temperature rose to 107° F., with very rapid pulse. He expired hours later. At necropsy, he was found to have aortic atherosclerosis, coronary atherosclerosis, and an old thrombotic occlusion of the right coronary artery.

Neuropathologic findings. There was a moderate degree of convolutional atrophy of the cerebrum. Basal vessels showed marked atherosclerosis with tortuosity. The lumen of the basilar artery was filled with a dry blood clot. This extended down and filled the lumen of the right vertebral artery. The left vertebral artery had a very narrow lumen due to extreme atherosclerotic thickening of its wall. Superiorly the blood clot reached the level of the superior cerebellar artery which was empty, but its orifice was sealed off by thrombus in the basilar. The right posterior cerebral artery had a mere pinpoint lumen with an extremely thick wall. The left cerebral peduncle was completely infarcted. The entire tegmentum of pons, cor-

ticospinal tracts, and the interpontine association tracts were involved in this massive softening (figures 1 B and C). On the left this malacia extended upward near the floor of the early portion of the aqueduct and on the right close to the lower edge of the mesencephalic nucleus of the fifth nerve. It also extended down through the pons to the beginning of the pyramids, both of which were transected by infarction. At the level of the olives, however, the pyramids were once again normal.

Comment. One of the most striking features in this case was the transient state simulating akinetic mutism lasting for four to five days. At the peak of this phase the patient gave the external appearance of apparent but not real coma, since he could still communicate with the outside world by volitional blinking of his eyes on command. The patient could follow the examiner around with his eyes, though he was unable to talk or move part of his limbs or move his face in gesture. The presence of a stenotic lumen of the right posterior cerebral artery makes the account of "flickering of light" before the patient's eyes and transient altitudinal hemianopic field defect meaningful. Likewise, obliteration of the openings of both superior cerebellar arteries by a thrombus would correlate well with the clinical finding of a fluctuating cerebellar type of incoordination associated with scanning speech. Unusual sleepiness and brief attacks of extensor spasms were both quite prominent in this case.

Case 2. A 53 year old white man had a history of sudden onset of nausea, vomiting, vertigo, and mental confusion on the day of admission. He had been hypertensive for about four to five years. Three years prior while talking over the telephone his speech suddenly became slurred, but he did not lose consciousness. When hospitalized he was found to have grade 2 hypertensive retinopathy, right central facial palsy, right twelfth nerve palsy, right hemiparesis, diminished abdominal reflexes on the right, hyperactive right knee jerk, and right extensor plantar response. He was discharged one month later, improved except for residual right-sided weakness and aphasic speech, predominantly of the motor type. One year later he suffered from a similar attack with some residual weakness on the right side and nominal aphasia.

At examination his temperature was 99° F., pulse 40 (sinus bradycardia), and blood pressure 140/90. Although able to answer a few simple questions and follow simple commands, he appeared lethargic, inattentive, and occasionally confused. He showed partial ptosis of the right lid and his right pupil was smaller than the left, but both reacted to light. There was conjugate deviation of the eyes to the left at rest. Volitionally he could not move his right eye to the right, while the left eye could move to the right with only slight limitation. His conjugate gaze in a vertical plane appeared intact. There was marked analgesia and anesthesia over right side of his face, with absent corneal reflex on the right. His jaw was deviated to the right. There was right facial weakness of peripheral type and his hearing was markedly impaired on the right. There was pronounced horizontal nystagmus at rest. He showed moderate dysphagia and dysarthria. His head was deviated to the left. There was moderate right hemiparesis. Reflexes were hyperactive on the right with bilateral extensor plantar responses. There was hypalgesia over the entire left half of the trunk and left extremities. Mild nuchal rigidity was found without positive Kernig sign. Sinus bradycardia, irregular respirations, and intermittent cyanosis were observed.

Lumbar puncture showed a trace of globulin, three cells, total protein 93 mg. per cent, negative Wassermann, and flat gold curve.

Clinical course. On the third hospital day he experienced increasing difficulty in swallowing. He suddenly expired from respiratory failure on the eleventh hospital day. Autopsy revealed generalized arteriosclerosis and coronary arteriosclerosis, with myocardial fibrosis. Aortic arteriosclerosis, arterio- and arteriolonephrosclerosis were found. There was hypertensive cardiovascular disease with cardiac hypertrophy; the heart weighed 800 gm.

Neuropathologic findings. The most outstanding observation was that of a thrombosed fusiform arteriosclerotic aneurysm of the basilar artery, associated with thrombotic occlusion of the right anterior inferior cerebellar artery. There was recent infarction involving the right cerebellar hemisphere and compression atrophy of the pons.

Comment. In light of the autopsy finding of a tortuous, arteriosclerotic aneurysm of the basilar trunk distorting and compressing the pons and most of the lower cranial nerves, one of two possibilities might explain the

clinical course of events. Either the S-shaped tortuous basilar aneurysm had shifted its position or else the cranial nerves at first tolerated gradual compression up to a certain critical point beyond which they became manifest clinically. There was no gross neurovascular anomaly at the base of the brain. Part of the patient's terminal episode might be correlated with the necropsy finding of right anterior inferior cerebellar occlusion, namely, right Horner's syndrome, right deafness, analgesia, thermanesthesia and hypesthesia over the right half of face, and contralateral hypalgesia over the trunk and extremities.

Case 3. A 63 year old man was admitted immediately following a convulsion. Three weeks prior to entry he experienced occasional dizzy spells, each lasting five to ten minutes. On admission he continued to show generalized convulsive movements. Examination revealed blood pressure 130/70, bilateral cataracts, and a soft, apical systolic murmur. Neurologic examination showed mild mental lethargy, disorientation as to time and place, spotty memory loss, dysphagia and bilateral diminution of gag reflex, hyperactive but symmetrical deep tendon reflexes with bilateral Hoffmann's sign, and left extensor plantar response.

Clinical course. During the first week he showed intermittent episodes of mental confusion, lethargy, disorientation, and memory loss for recent events. Between attacks he was rational, though somewhat drowsy. On the twelfth hospital day he experienced the onset of tingling and numbness of his left hand without demonstrable sensory deficit in the involved area, though his left arm and hand were generally weaker than those of the right side. Later the same day he suddenly could not understand what he saw when he read, nor could he recognize or name the different colors of objects around him. Printed words, figures, or shapes of objects ceased to have meaning. Hours later he was observed to breathe rapidly and deeply and soon became unresponsive. All four limbs became spastic and partially extended; his deep tendon reflexes were hyperactive throughout. There were abnormal plantar responses. Next day he remained comatose. His pupils were equal and his arms were in extension at the elbows, with both forearms pronated and wrists flexed. His deep tendon reflexes were bilaterally brisk with bilateral extensor plantar responses. Autopsy showed coronary arteriosclerosis, with stenosis of two anterior descending branches 3 cm. from the origin. There was moderate degree of aortic arteriosclerosis.

Neuropathologic findings. There was a 2 by 1.5 cm. area of recent softening at the posterior aspect of the left occipital lobe. Coronal section through the mid-brainstem revealed extensive softening traceable to the lower two-thirds of the brainstem structures. The basilar artery was occluded by a dark red clot adherent to the wall of the artery.

Comment. The occasional episodes of dizzy spells may represent evidence of early and mild circulatory disturbance involving the vestibular nuclei and their fiber pathways in the brainstem. His evanescent visual agnosia might be correlated with the finding of infarction in the posterior portion of the left occipital lobe. His terminal episode of tachypnea, hyperpnea, coma, decerebrate rigidity, and bilateral extensor plantar responses coincided with thrombotic occlusion of the main trunk of the basilar artery.

Case 4. A 74 year old man was admitted following a fall on day of entry. He had two previous episodes of "cerebrovascular accidents," three years and one year before, respectively, leaving no residuals. For two days previously his vision had been hazy.

Examination revealed blood pressure 230/100, pulse 78, and respirations 24. There was a grade 4 diastolic rough murmur, with loud and booming systole best heard over the apex. The pupils were unequal, the right larger than the left. Other findings included left medial rectus weakness and right central facial weakness.

Clinical course. Upon admission the patient showed mild left hemiparesis which cleared up completely by the following day. By the ninth hospital day he began to notice difficulty in swallowing. Examination on the same day revealed conjugate deviation of eyes to the left, right central facial weakness, and absence of gag reflex bilaterally. He lapsed into coma and expired. Autopsy showed generalized arteriosclerosis and rheumatic heart disease, with mitral stenosis and mural thrombus in the left atrium both old and recent.

Neuropathologic findings. The basilar artery was distended by a firm red thrombus which extended to the vertebral arteries. Horizontal sectioning of the brainstem showed an area of

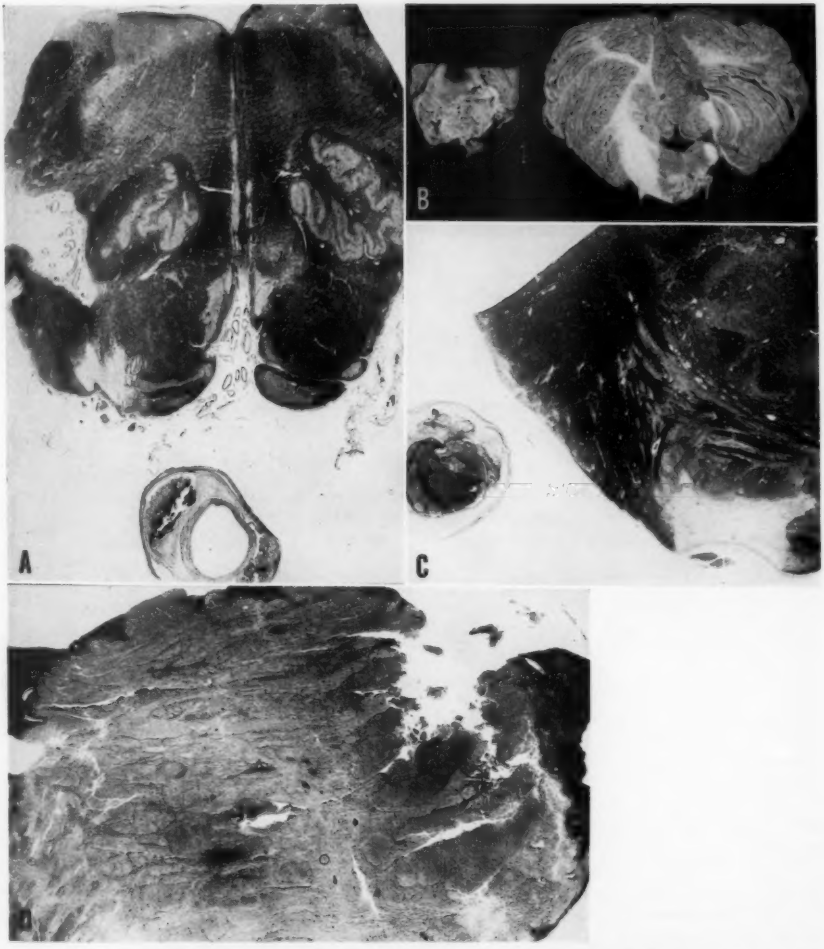

FIG. 1. *A.* (Case 7) Medulla at level of inferior olives showing extensive softening, cavitation, and patchy demyelination; cross section of basilar artery with atheromatous plaque and intramural hemorrhage. Weil myelin sheath stain.

B. (Case 1) Pons (left specimen) showing marked infarction necrosis involving the entire basis pontis and part of tegmentum; segment of basilar artery showing laminated thrombus (right specimen). Section of cerebellum and upper medulla showing infarction necrosis of the inferior olives and both pyramids.

C. (Case 1) Pons showing cavitation and softening over its right basilar portion; cavity partially filled with amorphous debris. Cross section of the basilar artery with its laminated thrombus was demonstrated. Weil myelin sheath stain.

D. (Case 7) Midpons showing pronounced demyelination and softening of its basilar portion. Weil myelin sheath stain.

malacia in the reticular substance of the pons on the left, inferior to the exit of the fifth nerve. At the level of the olives on the left, there was another area of softening (0.5 by 0.3 cm.) in the distribution of the left posterior inferior cerebellar artery (figure 2D).

Comment. The presence of left central facial paralysis, conjugate lateral gaze palsy, dysphagia, and bilateral abolition of gag reflex enabled clinical localization of the site of lesion at the left lower pons and upper medulla without much difficulty. Yet the absence of ipsilateral cerebellar dysfunction and characteristic "crossed" sensory defect of pontine lesion in the presence of rather extensive infarction necrosis of the lower brainstem was another example of the variability of clinical manifestations.

Case 5. A 61 year old man experienced sudden onset of right hemiplegia, right-sided numbness, slurred speech, and difficulty in swallowing two days prior to admission. He also had urinary incontinence and dizzy spells for many years. These attacks occurred without warning, lasting from minutes to hours.

Physical examination revealed blood pressure 160/90, pulse 68, and temperature 98° F. There was a low-pitched, slightly rough, grade 3 systolic murmur. Positive neurologic findings included slurred speech, bilateral absence of corneal reflexes, right central facial weakness, coarse horizontal nystagmus on lateral gaze, bilateral absence of gag reflex, inability to shrug the right shoulder, flaccid right hemiplegia, and hyperactive deep tendon reflexes bilaterally with bilateral extensor plantar responses. Cerebrospinal fluid findings were not remarkable except for total protein of 90 mg. per cent.

Clinical course. Right-sided weakness improved considerably on the third hospital day. Next day he suddenly lapsed into coma. Terminally he developed Cheyne-Stokes respirations, conjugate lateral gaze palsy, and rigid left limbs on passive movement.

At necropsy the basilar artery was filled throughout the length of the vessel by a recent, black thrombus. Sections through the vessel revealed that the lumen was narrowed in the central portion to approximately half its normal size by yellow atheromatous plaques and was completely occluded by the thrombus.

Comment. A long history of dizzy spells might be correlated with the finding of a markedly stenotic lumen of the central portion of the basilar trunk. The clinical course was rapidly fatal. The outstanding clinical features were fluctuating hemiplegia, conjugate lateral gaze palsy, coma, bilateral extensor plantar reflexes, and Cheyne-Stokes respirations.

Case 6. A 63 year old man was admitted following an episode of slurred speech and right-sided weakness on the night before entry. He was a known hypertensive for eight years. He was well until four months previously, when he noticed gradual onset of easy fatigability, followed in 24 hours by slurred speech, numbness of his right hand, and difficulty in walking. Five days later his right-sided weakness progressed to virtually complete paralysis and his speech also became unintelligible. His subsequent clinical course was static until the evening before his last admission when he was noted to stiffen, salivate, and become uncommunicative. His vital signs were: blood pressure 180/110, pulse 100, respirations 16, and temperature 98° F. Neurologic examination showed unintelligible speech, irregular and small pupils, right central facial weakness, bilateral diminution of gag reflex, right spastic hemiplegia, hyperactive deep tendon reflexes on the right, and right extensor plantar response. Cerebrospinal fluid findings were not remarkable except for total protein of 77 mg. per cent.

Clinical course. On the third hospital day the patient suddenly lapsed into coma. He developed stertorous breathing and flaccid quadriplegia. Terminally his temperature rose to 106.5° shortly before death.

At autopsy the basilar artery showed a severe degree of atherosclerosis and a markedly narrowed lumen which was completely occluded at its midportion by tan-colored thrombus. Horizontal sectioning of the brainstem revealed minute areas of old malacia within the right mid- and posterior pons.

Comment. The unusual feature in this case was convulsive disorder occurring as the presenting symptom. The onset of flaccid quadriplegia, stertorous breathing, coma, and terminal hyperthermia coincided with the beginning of an irreversible disturbance in the basivertebral circulation.

Case 7. A 61 year old man was admitted because of several "shaking spells." For the past two weeks the patient complained of generalized malaise, difficulty in controlling his arms,

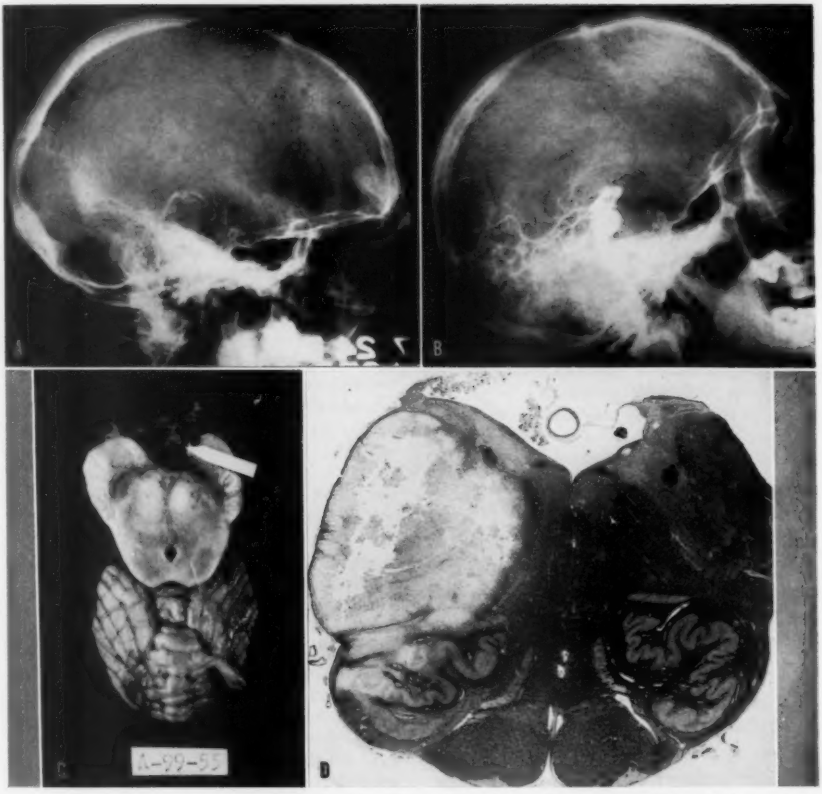

FIG. 2. *A.* (Case 9) Unretouched plain roentgenogram of skull. Lateral projection showing globular outline of the mass behind the dorsum sellae. Finger shadow over the anterior fossa is extraneous.
B. (Case 9) Unretouched vertebral angiogram showing the saccular bulge in the proximal segment of the basilar artery in its distal one-third and its scalloped aspect. Also note the posterior displacement of this vessel from its relation to the clivus.
C. (Case 8) Midbrain, cross section at level of red nucleus, showing an aneurysmal sac over the dorsal aspect of the cephalic end of the basilar artery in the interpeduncular space. White arrow points to the site of rupture of the aneurysmal sac.
D. (Case 4) Medulla at level of inferior olives showing marked softening and cavitation involving three-fourths of the dorsolateral medulla on the right including the dorsolateral portions of the right inferior olivary nucleus. Weil myelin sheath stain.

and numbness involving both arms. Two days prior he noted the onset of weakness and numbness of his right arm and leg. He also experienced difficulty in writing and in using his right arm. He dragged his right leg slightly in walking. He was unresponsive on arrival. His vital signs were blood pressure 185/70, pulse 96, and Cheyne-Stokes respirations. Neurologic examination revealed slight stiffness of neck; aniscoria, left pupil slightly larger than the right, but both reacted to light and accommodation; and increased muscle tone of the right limbs. Deep tendon reflexes were brisk throughout, with preponderance on the right. Plantar responses were extensor bilaterally.

Clinical course. The patient remained in

coma with stertorous breathing. On the fourth hospital day he developed increasing respiratory embarrassment which became irreversible a few hours later.

At autopsy the basilar artery was occluded by an extensive thrombus beginning approximately 0.3 cm. from the juncture of the vertebral arteries and extending to the level of the posterior cerebral arteries. The underlying pons appeared cystic, and on section it revealed a gelatinous, necrotic substance without apparent architecture (figure 1A and D).

Comment. Deep coma, rising temperature, and respiratory embarrassment immediately following repeated convulsive seizures were misleading, and they effectively prevented an accurate antemortem diagnosis. The lack of lateralizing or localizing sign that might suggest a pontine focus in this case was surprising in view of the extensive degree of infarction necrosis involving that structure.

b. Basilar artery aneurysm. From the standpoint of the morphology of the lesion and the problems involved in the differential diagnosis, three cases form a rather unique group. Case 2 of group *a* represents an example of a fusiform arteriosclerotic aneurysm of the basilar trunk that terminated by thrombotic occlusion. Clinically it ran a progressive and cumulative course of illness, characterized by multiple but asymmetric cranial nerve involvement and associated with lethargy and bilateral long tract signs in a manner indistinguishable from that of a space-consuming lesion in the posterior cranial fossa. Case 8 showed at necropsy a saccular aneurysm at the cephalic end of the basilar artery with subarachnoid leak; clinically it was marked by spontaneous subarachnoid bleeding, complicated by convulsive seizure, flaccid hemiplegia, coma, and death. Case 9 is a surviving instance of a spherical aneurysm involving the cephalic end of the basilar artery without rupture. Diagnosis was reached on the basis of roentgenologic finding of a calcified spherical shadow posterior to the sella on lateral projections of the skull and a subsequent observation of an aneurysmal mass in the course of the basilar artery on vertebral angiography.

Case 8. A 57 year old man experienced sudden onset of severe headaches associated with nausea and vomiting on the night before admission. He was in perfect health until one week before when he noted onset of constant occipital headaches and nuchal pain. On the night before admisison he experienced severe bandlike headaches about his entire head, followed by nausea and vomiting. He was a known hypertensive for two or three years. On arrival he was lethargic. Vital signs were temperature 98° F., pulse 92, and blood pressure 200/110. He was drowsy but able to answer questions. He had difficulty remembering dates and time. There was marked nuchal rigidity and slight blurring of nasal margins of both optic disks. His pupils were widely dilated, reacting sluggishly to light. He had a lumbar puncture and his spinal fluid was found to be grossly bloody, with I.P. 180 and F.P. 90. Two days before death repeat puncture showed I.P. of 240 and F.P. of 160; the fluid was xanthochromic.

Clinical course. During the first three days of hospitalization the patient appeared quite alert despite severe generalized headache and nuchal pains. Two days later he had an episode of increasing bifrontal and suboccipital headaches, associated with nausea, vomiting, perspiration, and rise in systemic blood pressure and pulse rate. Two days later headaches became quite severe and he was drowsy and voiced mildly paranoid ideas. For the next three days his headaches lessened in severity and he became very alert. By the eighteenth hospital day he suddenly complained of bifrontal and occipital headache; seconds later his speech became slurred, he slumped back to the pillow foaming at the mouth, and could not be reached. Almost immediately thereafter both upper extremities were forcibly flexed at the elbows and clonic movements began to involve both wrists, the left more so than the right; the lower limbs were extended rigidly throughout the attack. The entire episode lasted for about four and a half minutes, following which he remained unconscious for half an

hour and was incontinent of urine. As he emerged from the episode, his speech became markedly slurred, and he was confused and disoriented. There was increased stiffness of the neck, and the left central facial weakness became quite pronounced. He soon lapsed into coma. Next day he suddenly developed left-sided flaccid hemiplegia. During the last three days of life he was deeply comatose, with noisy respirations. His eyes rolled conjugately from side to side, and the plantar responses were bilaterally extensor. He expired suddenly on the twenty-first hospital day.

At autopsy there was a saccular aneurysmal dilatation measuring 3/16" by 1/8" in diameter at the cephalic end of the basilar trunk before its bifurcation into the posterior cerebral arteries. It was nestled in the recess between the medial margins of the cerebral peduncles with a blow-out on its anterior surface (figure 2C). There was an old infarct in the substance of the left half of the pons.

Comment. Clinically this case represented an example of spontaneous subarachnoid hemorrhage complicated by convulsive disorder occurring in a hypertensive subject. However, in retrospect, one is impressed with the recurring drowsiness and lethargy of considerable degree in the absence of sedation, the prominence of severe occipital headaches and nuchal pain, and the presence of pronounced extensor spasms in the lower extremities in repeated brief attacks.

Case 9. A 62 year old man was admitted with history of frequent falls and increasing dizziness of several months' duration. Eleven years prior to admission he suffered a cerebrovascular accident which left him with residual right-sided weakness and slurred speech. On examination his vital signs were: blood pressure 140/90, pulse 120, and temperature 102.6° F. He was emotionally labile. Positive neurologic findings included arteriosclerotic retinopathy, diminished corneal reflex on the right, right central facial weakness, right twelfth nerve weakness, slurred speech, difficulty in swallowing, right-sided weakness, hyperactive deep tendon reflexes, and bilateral extensor plantar responses. Cerebrospinal fluid findings were not remarkable except for total protein of 82 mg. per cent and a trace of globulin. He showed hyperactive left labyrinthine response on caloric testing. Weakness of vocal cords was demonstrated on laryngoscopy. A right vertebral angiogram revealed the presence of a large aneurysm situated at the upper end of the basilar artery, corresponding to the location of calcification present in the plain skull films (figure 2A and B). The lesion was considered inoperable and the patient was discharged.

Comment. An unusual instance of a nonleaking, spherical aneurysm of the basilar artery occurring in a normotensive man was diagnosed on the basis of vertebral angiographic findings. Clinically, the residuals of a previous stroke might suggest a supratentorial focus and the occurrence of emotional lability and dysphagia might be interpreted in terms of pseudobulbar symptoms. Yet the bilateral ninth and tenth and right twelfth cranial nerve involvement, bilateral extensor plantar responses, and dizziness strongly suggested brainstem structures as primarily and definitely implicated in the process.

NONVERIFIED CASES

c. Intermittent insufficiency syndrome of the basilar artery. This group consists of eight cases of circulatory disturbances involving brainstem structures. Clinically these cases provide for a broad spectrum of manifestations, ranging from transient repetitive attacks of paresthesias, weakness, dizziness or light-headedness, vertigo, dysphagia, or visual blurring with complete recovery after each episode, to recurrent events involving multiple cranial nerve nuclei and long fiber tracts of the brainstem with cumulative neurologic residuals after each successive attack.

Case 10. A 43 year old man was admitted because of transient episodes of numbness, left-sided weakness, and slurred speech, each lasting for two or three minutes for the previous five days. He was a known hypertensive of four months' duration. Two months later while on reserpine therapy he began to have "dizzy spells" associated with nausea, generalized weakness, and blurring of vision. Five days prior to admission he experienced transient left-sided weakness while getting out of bed. His condition resolved spontaneously in about five minutes. He continued to have four

to five similar episodes daily for four days before admission.

Examination revealed blood perssure 190/108, pulse 84, respirations 20, and temperature 99° F. Carotid pulsations were symmetric and equal bilaterally. On neurologic examination the patient was conscious and alert but anxious and apprehensive. He was oriented in all spheres. His speech was slurred. There was left central facial weakness and bilateral palatal weakness. He showed marked diminution in gag reflex bilaterally and left hemiparesis. There was slight preponderance of deep tendon reflexes on the left. Plantar response was extensor on the left. Sensation was grossly intact. The cerebrospinal fluid was essentially negative except for total protein of 100 mg. per cent.

Clinical course. On the night of admission the patient experienced transient left-sided numbness and developed slurred speech. On examination he was found to have partial left ptosis, pronounced left central facial weakness, weakness on turning his head to the left, inability to shrug his left shoulder against resistance, very weak left hand grip, and inability to raise his left arm against resistance. Left abdominal reflexes were absent. His left leg was also weak. This episode lasted for 40 minutes. Later that evening it was found that the patient also had left-sided hypesthesia and hypalgesia. Similar episodes continued to recur three to five times daily, each time with a little more residual weakness over the left side. By the eighth hospital day he began to have fewer attacks and there was partial return of motor function of the left leg. He still had residual left central facial weakness, left hemiparesis, and labile hypertension upon discharge.

Comment. The most outstanding features of this case were the frequency of transient episodes related to brainstem ischemia and the gradual cumulative neurologic residuals between these episodes.

Case 11. A 59 year old man was admitted with a history of sudden onset of transient numbness, weakness, and double vision three days prior to admission. He was a known diabetic of 13 years' duration. Three days prior he noticed onset of numbness involving the right side of his face and the perioral region, followed by numbness and tingling sensation of both upper extremities and the left lower extremity. This in turn was followed by weakness of the left upper and both lower limbs and transient dysphagia. He also noticed double vision. Within 24 hours from the time of onset weakness of the extremities was gone, and within 48 hours numbness and tingling sensations also subsided. However, he still had double vision upon admission.

At examination the vital signs were temperature 99.2° F., pulse 88, and blood pressure 160/100. There were scattered punctate hemorrhages in the right optic fundus. He was oriented but drowsy and wanted to sleep all the time. Memory was good for both remote and recent events. Pupils were not equal in size and did not react to light. There was bilateral ptosis, more marked on the right. Left Horner's syndrome was observed. Other ocular signs included paralysis of conjugate vertical gaze and limitation in conjugate lateral gaze, especially to the left; convergence was abolished. Motor function was grossly intact. There was partial facial nerve palsy on the left. Reflexes were sluggish but symmetric bilaterally. Sensation was grossly intact except for minimal vibratory sense impairment in the lower limbs.

Clinical course. For the first few days following admission the patient complained of drowsiness. Later there was some return of strength in his left arm and leg and his speech became more distinct, but he remained drowsy. The right pupil became dilated and fixed and left facial weakness persisted. Three weeks later he recovered almost completely from the initial episode, though he continued to complain of double vision.

Comment. This case demonstrated the intermittency and reversibility of multiple cranial nerve disturbances within the territory of supply of the basilar circulation, occurring in a diabetic of long standing. It is of considerable interest to note the prominence of drowsiness and abnormal sleepiness in this subject; the Parinaud syndrome characterized by paralysis of conjugate upward gaze, convergence paralysis, and limitation in conjugate lateral gaze (disturbances referable to lesion in the region of tectum of the midbrain at the level of the superior colluculi); and mild transient disturbance of the bulb, in the form of dysarthric speech and dysphagia.

Case 12. A 45 year old man was hospitalized because of dizziness, nausea, and vomiting of two days' duration. Two years prior to admission he suffered an attack of left supraorbital

pain, associated with dizziness, nausea, and vomiting. It left him with residual partial loss of sensation over the left side of his face. Three days before admission he had an attack of throbbing left supraorbital pain and diminution in hearing in his left ear. Next day he felt dizzy, light-headed, and nauseated; he vomited shortly thereafter. He also noticed marked accentuation of the residual numbness over the left side of his face since onset of present illness.

On examination the patient was lethargic but oriented. There was rapid nystagmus on both upward and conjugate lateral gaze. Corneal reflex was absent on the left. Hypesthesia and hypalgesia were demonstrated over the left side of the face. There was a Horner's syndrome on the left. There was left central facial weakness and Weber lateralized to the right. The remainder of the neurologic examination was normal. Lumbar puncture revealed grossly bloody fluid with xanthochromic supernatant.

Clinical course. On the night of the fourth hospital day the patient experienced an attack of severe headache over the left supra- and retroorbital regions radiating posteriorly toward the left ear. By the following morning examination revealed involvement of left fifth motor and left twelfth cranial nerves. Vertebral angiography was attempted without success. Bilateral carotid angiograms revealed no abnormalities. The patient was discharged home. On follow-up visits he complained of occasional left-sided headaches, and on examination he showed involvement of both the sensory and motor nuclei of the left fifth cranial nerve. His hearing deficit in the left ear and the left central facial weakness have disappeared.

Comment. A case of spontaneous subarachnoid hemorrhage is associated with multiple cranial nerve signs, all occurring on the same side. The character of headaches was consistent with that referred from the posterior fossa due to irritation of the tentorii cerebelli. Negative carotid angiography certainly did not exclude the possibility of an aneurysm or vascular anomaly in the posterior cranial fossa. The possibility of an aneurysmal mass arising from one of the long circumferential branches of the basilar artery (either anterior or posterior inferior cerebellar artery on the left side) in the vicinity of the left cerebellopontine angle could not be excluded.

Case 13. A 55 year old man entered with a history of sudden onset of buzzing noise in both ears of 17 days' duration. He also experienced light-headedness, blurred vision, nausea, and vomiting for two weeks. He was known to have hypertension for two years.

At examination his vital signs were: temperature 98.6° F., pulse 102, and blood pressure 160/100. There was a positive Rinné sign on the left and Weber lateralized to the open ear. Rotary nystagmus was present in primary position. Pupils were small and equal; they reacted to light, accommodation, and consensual stimulation. The remainder of the neurologic examination was not remarkable.

Clinical course. On the sixth hospital day the patient had an attack of nausea and vomiting without vertigo. On examination he showed nystagmus on looking to the right; numbness involving the right hand unaccompanied by objective sensory loss; right arm and leg weaker than the left. On the previous day he noted a transient decrease in hearing acuity in his left ear lasting an hour and a half, with complete recovery. By the sixteenth hospital day he had another episode of light-headedness at night, which resolved spontaneously. On one occasion his left arm and leg were found to be weaker than the right. A Mecholyl provocative test for pheochromocytoma was negative. He continued to have intermittent episodes of dizziness and blurred vision despite therapeutic efforts.

Comment. Initially the sudden onset of bilateral tinnitus associated with intermittent episodes of dizziness, light-headedness, vertigo, nausea, and vomiting would lead one to suspect Menière's syndrome. However, subsequent evolution of the illness clearly indicated that the patient was suffering from intermittent, recurring episodes of circulatory insufficiency principally involving the brainstem structures. Visual blurring might suggest insufficient blood supply to the visual cortex via the posterior cerebral vessels. There was an incomplete palsy of the left third nerve. The episodic vestibular disturbances and transient decrease in auditory acuity of the left ear might conceivably suggest an attentuation of blood supply to the left eighth cranial nerve via the left internal auditory artery. Alternating hemiparesis points toward basilar involvement.

Case 14. A 56 year old man was admitted with severe frontal headache and progressive loss of function of the right arm and leg of

one day's duration. For the past month he had noticed dizziness and light-headedness on rapid change of posture. On the day of admission he experienced severe frontal headache associated with nausea and vomiting. His speech also became thick and indistinct and he appeared drowsy. His vital signs were temperature 98.6° F., pulse 72, and blood pressure 200/100. There was a grade 3 systolic murmur over the aortic area which radiated into the pulmonic area and into the neck. The pupils were unequal, with the right pupil larger than the left, but both reacting to light and accommodation. Funduscopic examination showed arterial spasm and thickening of the retinal arterioles. There was left central facial weakness. The tongue was deviated to the right on full protrusion. He also showed paralysis of conjugate lateral gaze, more so to the left than to the right. Deep tendon reflexes were brisk, with preponderance on the right side. There was an extensor plantar response on the right. Motor function and sensation were both normal. Cerebrospinal fluid showed a trace of globulin and total protein of 89.5 mg. per cent.

Clinical course. Shortly after admission the patient developed difficulty in swallowing. When examined he appeared stuporous, with right hemiplegia and loss of sensation over left side of face and right half of the body. He was unable to look to the left on command and to the right only with difficulty. There were diminished corneal reflexes bilaterally and right central facial weakness. He had marked dysphagia and slurred speech. The gag reflex was absent bilaterally. Both legs were in extension. Bilateral extensor plantar responses were elicited. In view of the febrile course, leukocytosis, and presence of heart murmurs, repeated blood cultures were made with negative results. In the course of the ensuing two weeks he became afebrile and his speech became more distinct, but dysphagia remained. Six weeks after entry the patient began to notice improvement in swallowing.

Comment. The initial history of alcoholic excess, severe frontal headache, drowsiness, right-sided weakness, and slurred speech raised the question of an acute subdural hematoma. However, his subsequent clinical course rendered the previous diagnosis untenable. The development of a constellation of such signs as crossed sensory defect, right central seventh nerve palsy, bilateral absence of gag reflex, bilateral extensor plantar responses, and conjugate gaze palsy strongly suggest the brainstem as the principal seat of disturbance, with the pons bearing its brunt. The near complete resolution of cranial nerve dysfunction suggests a reversible state of intermittent circulatory insufficiency of the basilar arterial system.

Case 15. A 44 year old man was admitted because of sudden onset of dizziness and tendency to fall to the right. Three days prior he noticed aching pains in both shoulders and along the back of the right side of the neck. Those pains subsided gradually in the following two days but soon were followed by numbness in the right arm. On the following day he had a sudden attack of dizziness, with a tendency to fall to the right and gradual, increasing weakness involving his right arm and leg. He perspired profusely and mumbled indistinctly when attempting to speak, but he did not lose consciousness during that attack. On admission he felt dizzy only when asked to turn his head to the left; at that moment he became quite nauseated and vomited. He also complained of a diffuse, dull, aching headache, lessened on turning his head to the right. He was a known hypertensive of nine years' duration. On examination blood pressure was 160/110 mm. He appeared mildly lethargic, but oriented in all spheres. His speech was markedly slurred. He noticed diplopia on right lateral gaze. Nystagmus was present on looking to the right. He was unable to wrinkle his right forehead at will. The jaw was slightly deviated to the left. There was no demonstrable weakness. Reflexes were hyperactive throughout, with bilateral extensor plantar responses. There were slight hypesthesia and hypalgesia over the right forearm, otherwise not remarkable. Spinal fluid showed a trace of globulin and total protein of 79 mg. per cent.

Clinical course. He improved steadily during the second week. Upon discharge he still showed equivocal plantar response on the left, mild occasional dizzy sensation on sudden change in posture, and residual numbness in the right arm and forearm. All cranial nerve signs have since disappeared.

Comment. The significant features in this case were the reversibility and multiplicity of cranial nerve dysfunction, accentuation of dizziness and light-headedness on change in posture, presence of dull-aching diffuse headache,

and mental lethargy and bilateral extensor plantar responses.

Case 16. A 40 year old man was admitted with complaints of dizziness, nausea, vomiting, and unsteadiness of gait followed by paresthesias three days before. On the following morning the patient woke up with a numb right side of face, associated with weakness and incoordination involving his right upper and lower extremities. He was unable to maintain balance when sitting, standing, or walking without support, and he tended to fall to the right. He felt much more comfortable lying on his left side. Blood pressure was 170/110.

At examination he was conscious, alert, and cooperative. There were a partial convergence paralysis and mild nystagmus on conjugate right lateral gaze. Analgesia and anesthesia were found over the right half of face. Right corneal reflex was markedly diminished. His jaw tended to deviate to the right. There was some diminution in hearing in the left ear also. There was mild right hemiparesis. Gait was ataxic and broad-based, with tendency to veer to the right. Finger-to-nose and heel-to-shin tests were performed poorly on the right. Reflexes were brisk, symmetric, and equal bilaterally. Hypesthesia and hypalgesia were found over the entire right half of the body. Cerebrospinal fluid findings were not remarkable except for one-plus globulin and total protein of 91 mg. per cent.

Clinical course. By the fourth hospital day numbness over the right side of his body began to clear up, though the incoordination of his right limbs persisted. He continued to improve and was discharged home after three weeks. On a follow-up visit five months later it was found that hypesthesia over the right half of the face had since cleared. Incoordination of the right limbs was only minimal. Attacks of dizziness, nausea, and vomiting became less frequent and less severe.

Comment. Aside from recurring episodes of transient dizziness, light-headedness, nausea, and vomiting, the major part of the clinical picture could be ascribed to disturbances arising from the region of the upper pons and right cerebellar hemisphere.

Case 17. A 47 year old man was hospitalized because of sudden onset of severe dizziness, lightheadedness, unsteady gait, and double vision of 48 hours' duration. Two days before admission he suddenly experienced dizziness and double vision. He also noticed weakness and numbness involving the right arm and leg. He was nauseated and vomited several times. On the night before admission he developed difficulty in swallowing and his voice became quite hoarse. He was known to have hypertension for 10 to 15 years.

Examination showed blood pressure of 132/88. He was alert and oriented in all spheres. Pupils were unequal, with the right larger than the left. Other cranial nerve signs included vertical nystagmus, hypesthesia over left side of face, dysarthria, and dysphagia. There were right hemiplegia and right hemihypesthesia. Reflexes were brisk throughout, with bilateral extensor plantar responses.

Clinical course. Dysarthria and dysphagia cleared up rapidly. Sensation over the left side of face also recovered except for the upper half of the left forehead. There was some good functional return in the right limbs. However, the right-sided hypesthesia persisted. Despite clinical improvement, he continued to complain of recurring episodes of dizziness and easy fatigability.

Comment. Except for the occurrence of right hemiplegia, anisocoria, and bilateral extensor plantar responses, the remainder of the clinical picture would fit in nicely with the dorsolateral medullary syndrome (or the syndrome of the posterior inferior cerebellar artery) on the left.

REMARKS

These cases all show transient episodes indicative of insufficiency of circulation in the brainstem structures (dizziness, dysarthria), with or without insufficiency in the posterior cerebrals (visual blurring, blindness, mental lethargy, or confusion), followed in some (cases 15 and 17) by cumulative bilateral brainstem signs. The most striking features in case 10 are the frequency and the brevity of these episodes of paresthesias, weakness, dizziness, and slurred speech. Hypertension was present in six of the eight cases in this series. Prognosis in this group is not necessarily as grave as the symptoms at the peak of one attack might indicate.

TABLE 3

CEREBRAL ARTERIES INVOLVED IN VERIFIED CASES OF THROMBOTIC OCCLUSION

	Cases	*Per Cent*
Carotid Arterial System	31	57.5
Internal carotid	7	13.0
Middle cerebral	23	42.6
Common carotid	1	1.9
Basivertebral Arterial System	23	42.5
Vertebral	4	7.4
Posterior inferior cerebellar	2	3.7
Anterior inferior cerebellar	2	3.7
Superior cerebellar	2	3.7
Basilar, main trunk	8	14.8
Posterior cerebral	5	9.2

TABLE 4

CLINICAL MANIFESTATIONS OF BASILAR OCCLUSION

	Authors'	*Kubik and Adams*	*Siekert and Millikan*
Disturbed consciousness	7	18	10
Bilateral extensor plantars	5	9	–
Bulbar and pseudobulbar symptoms	6	5	18
Paralyses	7	18	23
Convulsions	5	1	4
Visual disturbances	4	5	5
Total number cases	7	18	28

DISCUSSION

In our experience softening occurred primarily in the brainstem in more than one-fourth of the entire group (56 out of 200 cases, or 28 per cent – tables 1 and 2). Similarly, out of 54 cases of demonstrable thrombotic occlusion of major cerebral arteries we have reviewed in our series, those involving parts of the basivertebral arterial system were found in 23 cases, or 42.5 per cent, and those involving the carotid system were observed in 31 cases, or 57.5 per cent (table 3). Since a significant proportion of cerebrovascular disease primarily involves brainstem structures, more so among older patient population, need for better understanding of the variability of clinical manifestations and gravity of prognosis seems imperative. Our present study has amply indicated such a need.

Basilar Arterial Occlusion

The general clinical characteristics of basilar artery occlusion are in keeping with those of Kubik and Adams[2] (18 verified cases) and Siekert and Millikan[9] (28 cases), namely: abrupt onset of episodic attacks of impaired state of awareness, ranging from drowsiness and stupor to coma, associated with various combinations of headache, dizziness, or light-headedness, diplopia or strabismus, nystagmus, blindness, nausea and vomiting, hemiplegia or quadriplegia, paresthesia or crossed sensory loss, pupillary abnormalities, dysarthria and/or dysphagia, incoordination, and bilateral extensor plantar responses (tables 4 and 5). However, from the phenomenologic standpoint, our series presents the following outstanding features:

1) A clinical state of altered awareness closely simulating that of the so-called "akinetic mutism." This was observed in case 1 of our series and lasted for approximately four days. During that period the patient was not comatose, but he showed flaccid quadriplegia and facial diplegia. He was totally anarthric and unable to move his head or neck. He was able to respond to simple verbal commands by opening or closing his eyes; the frequency of eye-blinking

TABLE 5

CLINICAL MANIFESTATIONS OF BASILAR OCCLUSION

	Authors'	*Kubik and Adams*	*Siekert and Millikan*
Pupillary changes	5	13	21
Paresthesias	4	4	4 (early)
Paralysis of conjugate gaze	4	1	8
Extensor spasms or decerebrate rigidity	2	3	15 & 3
Dizziness, vertigo	3	7	8
Hyperthermia	2	14	16

and the pauses between blinks were coded so as to convey slightly more complicated commands. Thus, the only remaining avenue of communication between this patient and his outside world was his ability to close his eyelids on volition. A comparable example can be found in Kubik and Adams'[2] paper in which they stated: ". . . In case 3 there was a curious and interesting condition where the patient seemed to hear and see but was powerless to respond by either word or gesture." This also occurred in case 3 of Biemond,[11] in which the cephalic end of the basilar artery was accidentally occluded during surgery on left acoustic neurinoma. Immediately following the occlusion for emergency hemostasis, the patient was already observed not answering questions. When she returned to the ward, she was then found to have developed total anarthria and tetraplegia, but she was not comatose and was able to follow the nurse with her eyes. An hour later she lapsed into coma and died at the end of four hours of acute ischemia of the brainstem. This inability to communicate is of special interest to the clinicians. It is highly unlikely that total anarthria as a part of the pseudobulbar syndrome could adequately explain the complete mutism and abolition of volitional control of the entire motor apparatus. Not only does it exist in such a disguised and subtle state that it often escapes careful analysis, but it also might furnish clues to the deeper understanding of the influence of functional integrity of brainstem structures on the state of awareness.

2) The frequent occurrence of convulsive disorder in our series, in contrast to only one instance reported in Kubik and Adams'[2] series and four out of 28 in Siekert and Millikan's[9] series, is worth mentioning in this regard. The occurrence of convulsions as a part of cerebral thrombosis is relatively infrequent. Millikan and Moersch[12] found eight out of 223 instances of focal cerebrovascular disease with convulsions, an incidence of 3.5 per cent. Dodge and co-workers[13] gave an incidence of 12.5 per cent (or 13 out of 104 consecutive autopsy-proven cases), whereas Brain[14] reported 18 out of 200 cases of cerebrovascular disease having epilepsy as the principal symptom, an incidence of 9 per cent.

3) Paralysis of conjugate gaze was observed in more than half of our cases; in one case in particular conjugate gaze palsy was the presenting complaint and it recurred later in the course of the illness.

4) Extensor spasms, or decerebrate rigidity, were observed in two of our cases, with periods of obvious increase in the tone of the extensor muscles of all four limbs occurring in spasms, lasting 10 to 15 minutes at a time, as part of terminal manifestations.

Careful analysis of our clinical data permits us to draw the following conclusion regarding the possible trend of the natural history of the basilar arterial disease. At least in some instances of basilar arterial occlusion by thrombosis, the terminal, irreversible event was preceded by repeated, intermittent episodes of circulatory failure, clinically taking the form of multiple cranial nerve palsies, mental confusion or lethargy, visual impairment, paresthesias, weakness to paralysis, pseudobulbar symptoms, and pyramidal involvement with partial to near complete recovery of function after each attack.

Basilar Arterial Aneurysms

While the number of cases included for this condition is far too small to permit an adequate coverage of the subject, each of the three cases presents a totally separate and distinct problem in clinical diagnosis. Case 2 is a verified instance of hypertensive arteriosclerotic fusiform aneurysm of the basilar trunk, associated with multiple asymmetric cranial nerve palsies, compressive atrophy of pons, bilateral damage of other brainstem structures, and terminal basilar occlusion by thrombosis. This case was unlike those reported by Dandy,[15] in which trigeminal neuralgia or Menière-like attacks were the principal complaints, or those reported by Denny-Brown and Foley[7] and Campbell and Keedy[16] in whom hemifacial spasm, sudden unilateral or bilateral auditory loss, or facial weakness of the peripheral type played prominent rôles. Case 8 presents the clinical picture of spontaneous subarachnoid hemorrhage, complicated by convulsive disorder, marked suboccipital headaches and nuchal pains, periodic disturbances in respiratory rhythm, labile hypertension, and terminal episodes of extensor spasms involving all four limbs. At necropsy a small saccular aneurysm the size of a peppercorn was found over the posterior surface of the cephalic end of the basilar trunk, ruptured over its anterior aspect. Case 9 represents an unusual example of unruptured spherical aneurysm of the cephalic end of the basilar artery pressing upon the brainstem structures. Definitive clinical diagnosis was achieved through demonstration of the aneurysmal mass in the proximal segment of the vessel by vertebral angiography and by plain roentgenogram of the skull showing globular outline of the calcified mass behind the dorsum sellae. The clinical significance of these unruptured, large basilar aneurysms is the close resemblance they may bear to posterior fossa neoplasms in their insidious but cumulative clinical course. Case 8 in Richardson and Hyland's[17] series belonged to the same category as our case 9 except that in the former, the unruptured aneurysm took origin from the vertebral trunk instead.

Basilar Insufficiency States

The inclusion of clinical data on four of the seven resolving cases of basilar arterial occlusion by Kubik and Adams[2] served to stimulate many case reports on this subject. That the presence of stenosis of the basilar lumen may in part be responsible for the production of transient episodes of mild brainstem dysfunction has been suggested by Denny-Brown[3] and later confirmed by Silversides[18] and in two of our verified cases of basilar arterial occlusion. The former author emphasized the clinical significance of the syndrome of intermittent basilar insufficiency, which is characterized by periodic disorientation, dizziness or light-headedness, speech defect, blindness, and fleeting bilateral brainstem signs. According to Denny-Brown, it is the presence of preexisting arterial disease (atherosclerosis) that interferes with the compensatory hemodynamic mechanisms through anastomotic circulation rather than the transient cerebral vasospasm that is to account for the evanescent nature of the clinical features in these vascular states.

Our group of eight cases of circulatory insufficiency involving the brainstem structures presents a fairly wide spectrum of clinical manifestations. No obvious precipitating or exciting factors common to most of the cases were found. Age of the subject, nature as well as the

site of the lesion do not as a rule seem to be the crucial factors in the prognosis of these insufficiency states. However, we have found that the number of previous cerebral episodes, the neurologic deficits between attacks, and the circumstances that brought about lowered body resistance or fall in systemic blood pressure influence the immediate prognosis of those cases. Such predisposing factors as excessive fatigue following overexertion, blood-letting, surgical shock from blood loss, postural hypotension, and syncopal attacks are effective in bringing about instability of the brainstem circulation.

SUMMARY AND CONCLUSIONS

1. The authors present seven verified cases of basilar arterial occlusion, three cases of basilar arterial aneurysm, and eight cases of basilar circulatory insufficiency states.

2. Vascular episodes involving the basilar artery (occlusive, aneurysmal, or intermittent insufficiency in type) occur more frequently than is generally realized.

3. Emphasis is placed upon the prominence of altered state of awareness, bilateral hemiparesis to hemiplegia, convulsive disorder, conjugate gaze palsies, bulbar or pseudobulbar paralysis, and visual impairment in our verified series of basilar occlusion. The protean nature of the clinical manifestations in circulatory insufficiency affecting brainstem structure is similarly stressed.

4. Grave prognosis and relatively higher fatality rate in instances of basilar occlusion would justify the consideration of a more active and direct therapeutic approach to such clinical problems.

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Regeneration in the Cord of Spinal Monkeys

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THE SUBJECT of regeneration in the central nervous system has been reviewed recently.[1] During the last few years several investigators have demonstrated that transected intramedullary nerve fibers can regenerate in rodents and carnivores, notably in those animals to which pyrogenic bacterial polysaccharides were administered after severing the spinal cord.[2–4] Central nervous regeneration takes place with great facility in lower species, such as fishes, newts, and salamanders.[1] Does it occur at all in higher species? Little information is available for primates. No experimental studies in monkeys comparable with those in rodents[5] and carnivores have been reported.

MATERIALS AND METHODS

Ten African green *(Cercopithecus)* monkeys weighing 1.3 to 2.6 kg. comprised the first series. They were grouped in pairs according to weight and sex. They were anesthetized with Nembutal (30 to 40 mg./kg.) and laminectomies were performed at T12 to L2. Transections were made as near the level of the lower motor neurons of the hind limbs as appeared compatible with avoiding disturbance of vascular supply, in an effort to keep distances necessary for regeneration as short as possible. The dura mater was incised longitudinally for 2.0 to 2.5 cm. and a special, blunt-tipped, curved seeker was slipped subdurally around the spinal cord. The cord was then severed with several light strokes of a thin scalpel to avoid compression and traction, and the seeker was lifted dorsally through this incision. The operative field was kept moist with Elliott's solution B and blood and clots were removed from the dural sheath with suction. The cut surfaces of the spinal cord were inspected and brought into as close apposition as possible within the dura mater. The dural incision was left unsutured but a Gelfoam strip was laid over it and the muscle, fascia, and skin wound closed. Levels of laminectomy were verified radiographically in these monkeys.

The basic operative procedure was altered in a second series of six African green and two Philippine *(Cynomolgus)* monkeys. Laminectomy was performed as previously, and over the ex-

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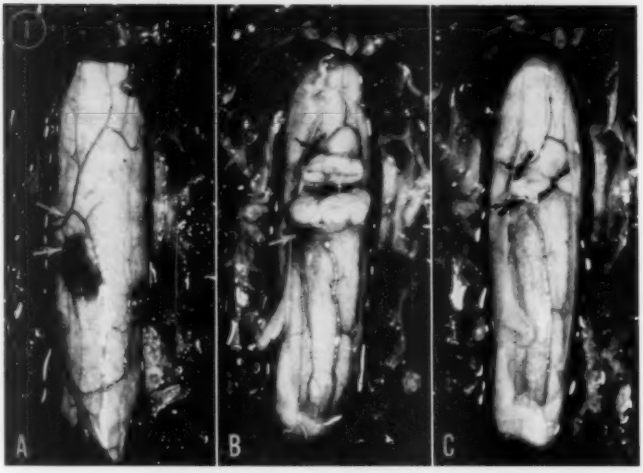

FIG. 1. Photographs taken with the speedlight unit of the Zeiss "Otoscope" during an operation. The cord is exposed in *A*. In preparation for ligating one of the dorsolateral arteries (arrows) a small hemorrhage developed. In *B* the vessels (arrows) have been ligated and the cord sectioned. Note the "mushrooming" of white matter. In *C* the stumps are being apposed; one suture (right) has been placed through pia mater. Magnification approximately 2.5x.

posed cord the dorsal vessels were ligated or coagulated and the ventral spinal artery was spared (figure 1). Some of the pia mater on the ventral and lateral aspects of the cord was left intact and that over the dorsal columns was sutured in two or three places with 6-0 silk thread to overcome the tendency of the stumps to "mushroom" (figure 1B). This operation involved slower dissection through the spinal cord and required 40 minutes or more, in contrast to approximately 30 minutes for the basic procedure, but it resulted in better apposition of the cord stumps. In the last two African green monkeys the transection was performed at T8 and T9 and no Gelfoam was used.

In one monkey a second operation was performed 340 days after the original transection. The transecting scar and a few millimeters of the spinal cord on either side were resected. It proved impossible to reunite the newly formed stumps and the animal was killed.

A strict regimen of postoperative care was adopted. All animals were given daily attention without interruption by holidays. Care included manual expression of urine until evacuation became automatic, massage and exercise of hind limbs, cleaning and drying soiled surfaces, and dressing wounds and ulcers. They were kept in air conditioned quarters in which no extremes of temperature occurred. Cages measured inside 15½ by 18 by 24 inches; the floors were covered with sponge rubber mattresses encased in soft cloth covers which were changed daily or oftener as necessary. Unlike spinal cats, the monkeys usually disturbed their bedding and frequently preferred to lie on the metal floor, behavior which predisposed toward ulcer

formation on ankles and rumps. Diet was varied and mixed, consisting of fruit, greens, root vegetables, cereal, milk, occasionally eggs or meat, and cod liver oil.

Maintenance of health was a greater problem in spinal monkeys than in spinal cats. Only three of the 18 animals developed no ulcers from pressure, friction, or cannibalism. Six chewed the hind feet or tail at one time or another; two of these deteriorated and became debilitated in consequence. Six monkeys developed friction ulcers on the ankles; five had decubiti on the rumps and anal regions; the latter type of wound was especially troublesome. In most instances, local medication, bandaging, and administration of antibiotics proved adequate to control and heal ulcers and self-inflicted wounds. In six cases the ulcers were refractory and in one monkey they contributed to death after ten months' time. Another animal died of unknown cause at five months. Bladder infection was encountered in one animal, a control monkey, about one week after operation. It seemed to be resistant to treatment with Erythrocin but healed after several weeks of treatment with other antibiotics. Organisms found in the urine were a beta-hemolytic streptococcus and a Proteus. Another animal had bloody stools for a few days.

Piromen* was given intravenously each day to one member of each pair, selected according to weight and sex, beginning immediately after operation and continuing for two or three weeks or until evidence of tolerance appeared. Therapy was then discontinued for two weeks and resumed at the original dosage. The initial dose was 1.0 μg./kg. body weight and this was increased to 1.5 μg. and 2.0 μg. from time to time in an effort to maintain febrile responses and changes in leukocyte counts, which served as indices of the drug's activity.

All but one monkey of the second series received Piromen intravenously, beginning at 5 μg./kg. body weight and increasing to 10, 50, and 100 μg./kg. as indicated by febrile reaction and by changes in total number of circulating leukocytes. Here, too, intervals without therapy were interspersed with periods of treatment. In one of the two animals killed at eight weeks, the drug was given intraperitoneally after the first week when difficulty in entering veins was encountered.

Rectal temperatures were recorded before and at intervals after Piromen administration. It was rarely possible to avoid exciting the animals and this raised their temperatures. The zero hour temperatures, under the most satisfactory standard conditions, varied from 101.0° to 101.5° F. (slightly less in *M. Cynomolgus*). Responses to Piromen were variable; a rise usually occurred about one hour after administration, amounting to 1.1° F. on the average.

Total leukocyte counts were made at the time of Piromen administration and usually at one-half or one hour and three or four hours later. Blood was drawn from fresh stab wounds of ears or tail or from the veins of the extremities. Piromen administration in adequate doses was followed by a leukopenia at 30 minutes to one hour, the decrease usually amounting to 30 to 50 per cent. A leukocytosis sometimes ensued at three hours after Piromen administration, but excitement alone often led to

*A bacterial polysaccharide obtained from a Pseudomonas species; manufactured by Baxter Laboratories, Inc.

a rise in the cell count at one to three hours. In the animals given high doses of Piromen (100 μg./kg.) leukocytosis occurred at one hour and occasionally reached 200 per cent or more of the basal value.

To control excitement, an intact African green monkey was rendered tranquil with Serpasil daily in oral doses increasing from 2 to 10 mg./kg. body weight. Handling did not alter the total leukocyte count significantly, but Piromen in doses of 0.5 μg./kg. brought about the characteristic leukopenia at 30 minutes to one hour.

Duration of the experiments varied from 57 to 350 days. The animals were killed with Nembutal and the appropriate segments of the spinal cord removed. Some were immersed in 10 per cent formalin and imbedded in paraffin for staining with protargol, and others were fixed in ammoniated absolute alcohol for the pyridine silver method. Perfusion-fixation was employed in two instances. All specimens were sectioned serially in parasagittal planes.

RESULTS

Scars formed between the severed ends of the spinal cord in all monkeys. These varied in density and were thinnest in regions of close apposition in the animals in which the stumps had been sutured and the principal arteries spared. Even in cases of close approximation, the fibroblastic reaction was marked. In no case did we succeed in excluding collagenous fibers from the wound and the density of the scar increased with time. In none of the monkeys did neuroglia form a discrete barrier over the cut ends of the cord. Furthermore, there appeared to be little difference between treated and nontreated animals in respect to the cellularity of the matrix of the spinal cord wound. The animal with the urinary tract infection had the most cellular scar. In the animals which had received Piromen, scars seemed less discrete and

TABLE 1
SUMMARY OF EXPERIMENTS

Monkey				Conditions at Operation				Histologic Observations		
No.	Sex	Weight (kg.)	Duration (days)	Level	Apposition	Hemorrhage	Therapy	Necrosis or Cavitation	Scar	Intraspinal Regeneration
1	Female	1.4	163	L-1	Good	+++	Piromen	++	++	±
2	Female	1.3	163	L-1	Excellent	++	None	+	+	—
3	Male	1.3	148	L-1	Good	++	Piromen	+++	++	—
4	Male	1.5	146	L-1	Good	++	None	++	++	—
5	Female	1.5	145	L-1	Excellent	+	Piromen	+	+++	±
6	Female	1.5	145	T-12	Very good	++	None	+	+++	—
7	Male	1.6	157	L-1	Very good	±	Piromen	++	++	+
8	Male	1.6	157	L-1	Good	+	None	++	++	—
9	Male	2.3	140	L-2	Fair	++++	Piromen	+++	++	—
10	Male	2.7	140	L-2	Poor	++++	None	+++	+++	—
11	Female	2.2	340	T-12	Sutured	±	Piromen	±	++	±
12	Female	1.8	223	L-1	Sutured	±	Piromen	±	+	±
13	Female	3.2	161	L-1	Sutured	++	Piromen	+	++	••
14	Female	3.8	307	L-1	Sutured	±	Piromen	±	+	+
15	Female	3.6	90	L-1	Sutured	++	Piromen	±	+	±
16	Female	3.3	90	L-1	Sutured	+	Piromen	+	+	+
18	Male	1.7	57	T-9	Sutured	±	None*	+	+	±
20	Male	1.5	57	T-8	Sutured	±	Piromen	+	+	±

*Persistent urinary tract infection.
**Advanced postmortem autolysis.

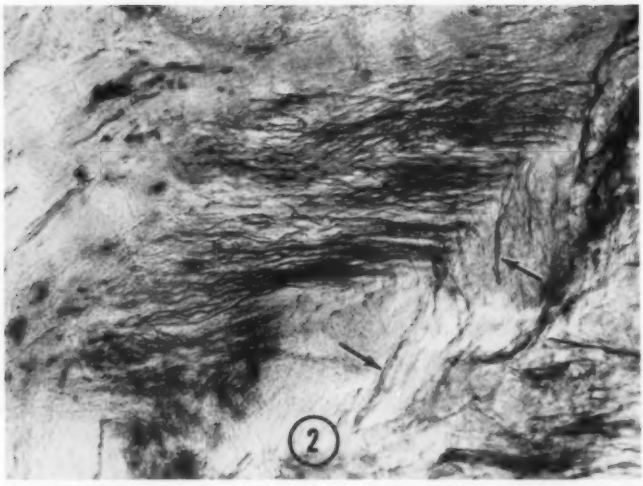

FIG. 2. Photomicrograph of a bundle of nerve root fibers of extramedullary origin running horizontally in the scar of monkey 7. Intraspinal regenerating fibers, some in process of degeneration, are shown at right angles to the root fibers at the arrows. Pyridine silver stain; magnification 300x.

blended with the cord parenchyma more than in the controls but there was considerable individual variation. Less necrosis and cavitation were found in the spinal cords which had been sutured than in those which had not. The greatest damage occurred in those in which there had been the most severe spinal cord hemorrhage at operation.

Many preparations showed regenerating extramedullary spinal nerve root fibers in the scar tissue surrounding the spinal cord at the transection site and in the scar uniting the two stumps. Root fibers were not observed in the monkeys sacrificed 90 days or less after operation. Little or no relationship between amount of trauma and spinal root regeneration could be observed. Piromen appeared to have had no effect on this. Orientation of regenerating fibers occurred along connective tissue fiber bundles into the scar and, with the exception of monkeys 7 and 16, rarely did fibers enter the spinal cord parenchyma. Figure 2 shows a large fascicle of dorsal root fibers which have regenerated into the transecting scar of monkey 7.

No unquestionable regeneration of intraspinal neurons could be observed in five of the six untreated monkeys' spinal cords. The only one which seemed to have any regeneration was that which had a urinary tract infection. Figure 3 shows fibers entering the scar from the caudal stump over strands of young fibrous connective tissue. In other control animals thickened ends of severed fibers were often found terminating not far from the transecting scar. If these had at any earlier time exhibited abortive regeneration, it was no longer in evidence. The contrast between active regeneration of spinal root fibers and lack of regeneration of the intramedullary neurons was striking.

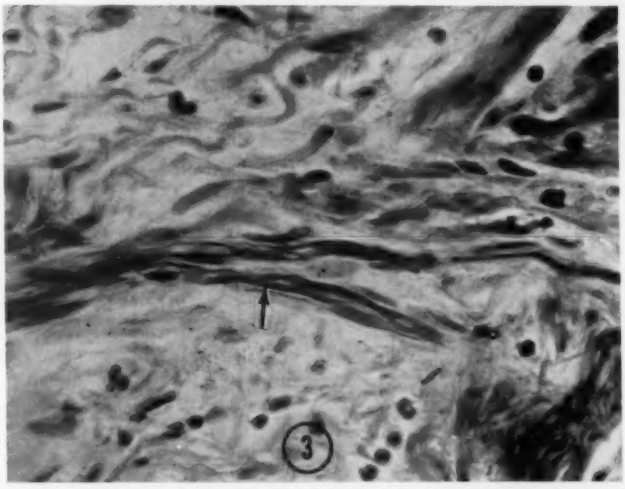

FIG. 3. Photomicrograph of a small fascicle of fine regenerating intraspinal neurons accompanying a strand of young fibroblasts. The neurons, shown at the arrow, arose in the ventral funiculus of the caudal stump and passed rostrad (to the right in the figure) into the transection scar. Monkey 18; protargol stain; magnification 580x.

In nine of the 12 Piromen-treated monkeys there appeared to be, or to have been, some regenerating intraspinal neurons, but in most instances these were few; an occasional fiber or a small group of fibers could be traced from one stump or the other into the transecting scar. Regeneration was no more than abortive in most of the animals. A great number of regenerating fibers appeared in the scar of monkey 16. Most coursed for short distances and none could be traced with certainty across the transection. Two of the Piromen-treated spinal monkeys showed no sign of intramedullary regeneration; these were animals with extensive necrosis in the cord stumps. One other specimen (M 13) could not be evaluated because of advanced postmortem autolysis.

The most impressive regeneration was seen in monkey 7, 157 days after operation. The collagenous tissue of the scar had become dense in this animal. Lateral funiculus neurons of one side were observed to pass deeply into the blending scar tissue of the transection, twisting and turning with the collagenous fibers. Some ended in little bulbs in the scar. Regenerating fibers from both rostral and caudal stumps entered the scar. Continuity through the scar could not be traced in any one section but scattered small fascicles and pieces of individual nerve fibers occurred serially in many sections (figure 4). Some of these appeared to be in process of degeneration. They were beaded, as shown in figure 4B, and represented regenerated neurons being destroyed by pressure of the collagenous scar. One gained the impression that more continuity had existed some time earlier, before the scar had become so dense.

Functional restitution was not observed at any time after spinal cord transection in the monkeys. There was only one observation which even suggested hope that some function might be returning. This occurred 85 days after operation in monkey 7 and consisted of movements of one leg and foot which appeared to be purposeful and which differed in quality from those commonly elicited reflexly.

COMMENTS

In previous studies in the cat,[2,3] the use of Piromen seemed to inhibit the formation of a superficial glial membrane and it was thought that the successful regeneration of intraspinal neurons may have come about in consequence of this. In the present experiments with monkeys the glial response was less in evidence than in the cat. The fibroblastic reaction was more severe and, even when nearly perfect apposition of the stumps was achieved, collagenous tissue made its way between the ends. Although it seemed that the Piromen-treated specimens showed somewhat more blending of scar with cord parenchyma than the controls, the amount of regeneration of intraspinal neurons that occurred was slight in most instances. Despite the lack of heavy marginal gliosis the process of regeneration was minimal. This was true for the entire series – 57 through 350 days.

The few regenerating nerve fibers seen in most treated specimens followed young connective tissue cells and fibers, as was noted previously,[4] but a highly cellular tissue matrix thought to be favorable to regeneration in the cat was not as pronounced in the monkey. Even though there was no marked difference between treated and control monkeys in respect to cellularity of the wound, most controls showed no intraspinal regeneration and the Piromen-treated monkeys rarely showed more than abortive regeneration. We are left with the impression that intraspinal neurons of these primates under the conditions of our experiment lacked potentialities for regeneration to the same degree encountered in rodents[5] and carnivores.[2–4]

The most favorable instances of intraspinal regeneration in the monkey occurred in animals which had been treated with Piromen. The only instance in which a control animal likewise showed some regeneration was one which had had a bladder infection with organisms known to be highly pyrogenic. A possible role of intercurrent infections in central nervous regeneration has been discussed elsewhere.[1]

As was seen in the chronic spinal cats,[1] collagenous scar tissue tended to increase in density with time and appeared to block what little intraspinal regeneration had occurred at an earlier period. In the monkey the encroachment of fibroblasts and the formation of scar tissue in the wound was more pronounced, even with Piromen therapy, than it was in the best experiments with cats. The scar tissue readily served as a guide to regenerating peripheral nerve fibers which grew into the region of the scar. There was no lack of potential for regeneration by extramedullary spinal nerve root fibers even though intraspinal neurons showed little growth.

CONCLUSIONS

On the basis of the present series of experiments, it is concluded that some regeneration of intraspinal neurons occurred in spinal monkeys under therapy with Piromen which, in some way,

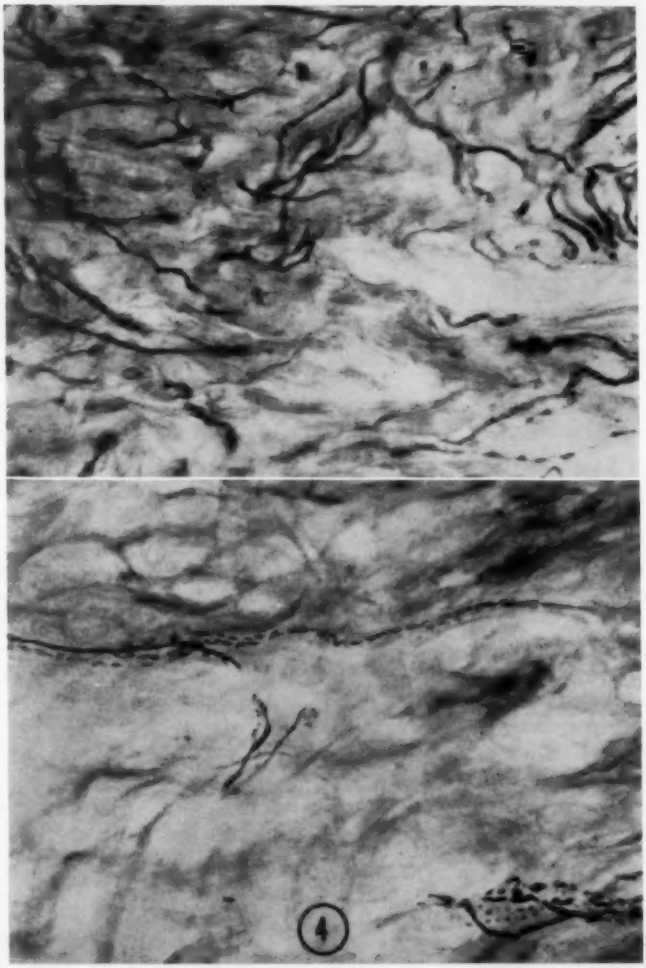

FIG. 4. Photomicrographs of intraspinal neurons which appear to have regenerated into the transection scar of monkey 7. *A*, neurons descending from the lateral funiculus of the rostral stump. *B*, thin nerve fibers in the scar ascending from the caudal stump and undergoing degeneration; note the beaded character of some. Pyridine silver stain; magnification 580x.

played a permissive role. Even under the most favorable conditions, regeneration of intraspinal neurons was slight in contrast with that in cats and with that of extramedullary spinal nerve root fibers. The intraspinal fibers were soon choked off by a dense collagenous scar and no functional restitution ensued.

Experiments were initiated in 1952 at Baxter Laboratories, Morton Grove, Illinois, and transferred in 1954 to the National Institutes of Health. Many people participated at one time or another. We are pleased to acknowledge assistance in various phases of the study by W. F. Agnew, Anne Campbell, Elizabeth Dorrill, E. R. Feringa, M. P. McQuillen, Ruth Seckara, and Polly Weiss. Photomicrographs were prepared by L. T. Pimental.
Elliott's solution B was prepared by Baxter Laboratories of Canada, Ltd., Acton, Ontario.
We thank Dr. J. A. Schneider of Ciba Pharmaceutical Products, Inc. for Serpasil used in this study.

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■ After having divided transversely the two posterior columns of the spinal cord in the dorsal region, in a dog, we cover its eyes and wait until it has lain down in a state of quietness. When it seems to be perfectly quiet, we find, if we gently touch the skin of one of its hind toes, that it lifts up its head and tries to see what is the cause of the irritation. It is certainly difficult to decide what kind of sensation this dog has felt, but I think I may show that it is a tactile sensation. Before discussing this point, however, I must say that it is not in consequence of a local reflex movement, shaking the whole body, that the animal looks anxiously around it. If it were so, the movement of the head would not take place immediately after the irritation and at the very same time that the irritated leg is withdrawn. Besides, after a complete transversal section of the spinal cord, when reflex movements are much stronger than after a section of the posterior columns, the head of the animal does not move at the time we touch the under part of its hind toes. Therefore, the dog, in our experiment, moves its head because the touching of its toes has directly given a sensation. When we think that there is a real hyperaesthesia in these toes, it seems possible that the simple touching of the toes is painful; but the hyperaesthesia, I think, is not of a sufficient degree for the production of pain from such a trifling cause. Still more, the touching of other parts of the skin of the posterior limbs, which are endowed with the same morbid power of causing pain as the skin of the toes, is the same morbid power of causing pain as the skin of the toes, is not followed by a movement of the head; so that it becomes very probably that the effect following the touching of the toes depends upon the propagation of a tactile impression to the encephalon, the skin of the toes being endowed with more tactile sensibility than that of the legs. The posterior columns, therefore, seem not to be the only channels of the tactile impressions.

C. E. Brown-Séquard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

Xenon in Encephalography

C. B. Pittinger, M.D., E. F. Van Epps, M.D.
and R. A. Utterback, M.D.

Recognition of the morbidity subsequent to pneumoencephalography has resulted in efforts to find a more suitable replacement agent than air. The effects subsequent to the subarachnoid injection of a large variety of gases and vapors in animals and human beings have been reported. Analgesia as a theoretical concomitant effect was a consideration in studies involving anesthetic agents as substitutes for air injection.

Jungling[1] and Denk[2] were among the first to substitute oxygen for air replacement, and others have since advocated the use of this gas in encephalography with various degrees of enthusiasm.

Liberson[3] reported the use of carbon dioxide, nitrogen, and helium in human encephalography. Severe reactions encountered with the use of carbon dioxide were attributed to its high solubility. Helium was considered superior to nitrogen as a substitute for air in decreasing postencephalographic distress.

Aird[4,5] reported on a controlled study of experimental encephalography with anesthetic agents in dogs. Among the agents studied for their effects after subarachnoid injection were acetylene, cyclopropane, divinyl oxide, ether, ethyl chloride, ethylene, nitrous oxide, and vinyl chloride. Severe toxic effects and even death resulted from the use of some of the agents, notably the volatile ones. On the basis of this study, nitrous oxide and ethylene were considered ideal agents for encephalography.

Newman[6] reported unsatisfactory roentgenographic results from the use of nitrous oxide in human encephalography. Preliminary results with ethylene were encouraging, and a series of 30 human encephalograms with this gas were reported[7] with claims of an appreciable decrease in the severity and duration of postencephalographic headache. Recognition of the explosive hazard associated with the use of ethylene, especially if immediate craniotomy were indicated, suggested the possible utility of a nonexplosive gas with the same solubility properties as ethylene.

Cleveland and End[8] in their report of encephalography with helium considered the two following factors responsible for the rate of passage of an inert gas from the subarachnoid space into the blood stream: 1) differences in the tensions of the gas within the subarachnoid space and arterial blood,

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and 2) the inherent diffusibility of the gas. However, since the gas passes from the ventricles to the blood stream through a wet tissue barrier, consideration of solubility is an important factor. Indeed, Jones[9] has reported convincing evidence that the in vivo rate of exchange of inert gases between blood and tissue is primarily a function of solubility and blood-tissue perfusion rate.

The water solubilities of ethylene and xenon in terms of Henry's Law constant $x10^{-7}$ are 1.21 and 1.12, respectively, at 38° C.[10] This marked similarity of solubilities of these two gases and the encouraging reports[4-7] incident to the use of ethylene in encephalography suggested the possible usefulness of xenon for the same purpose.

Xenon is a colorless, tasteless, odorless, and nonexplosive gas which is present in infinitesimal amounts in the atmosphere. Because of its relative chemical inertness, it is classified as one of the "inert" or "noble" gases. It has been shown to be pharmacologically active as a central nervous system depressant in human beings by Cullen and Gross,[11] who first reported its use as an inhalation anesthetic agent. In a clincopathologic study of patients anesthetized with xenon, Pittinger and co-workers[12] reported evidence of only minor effects upon biochemical and physiologic processes.

This preliminary study of xenon encephalography was made 1) to determine the quality of roentgenographic results obtainable, 2) to obtain information regarding the persistence of gas within the ventricles after injection, and 3) to observe the patients for clinical evidence of central nervous system effects, especially sedation, hypnosis, and respiratory depression.

PROCEDURE

Ten patients were premedicated as for air encephalography, and lumbar puncture was performed with an 18-gauge needle with the patient in the sitting position. Two three-way stopcocks connected in series were attached to the needle in order to facilitate manometric pressure readings, withdrawal of spinal fluid into a 20 ml. syringe, and injection of xenon from a 50 ml. syringe.

The outlet of the gas cylinder was cleaned with alcohol, allowed to dry, and then fitted with a short piece of sterilized, thick-walled rubber tubing. After flushing the air from the tubing with xenon, the end was clamped. Xenon was conveniently removed for use into 50 ml. sterile syringes through an attached 25-gauge needle inserted through the side of the clamped rubber tubing containing the gas under slight pressure.

The desired amount of xenon was injected into the lumbar subarachnoid space in small increments, usually 10 ml., after removal of an equivalent amount of spinal fluid. Manometric readings were made in some of the procedures after each addition of gas.

Roentgenograms were made about 15 minutes after completion of the injection of the gas, and in some cases additional films were made after longer periods to estimate the movement of the gas from the ventricles.

EXPERIMENTAL DATA AND RESULTS

The clinical data and roentgenographic results are included in the following case histories which contain references to the appropriate photographs (figures 1 to 18) of the roentgenograms obtained in the study. Obviously, not all of the views taken in the course of a routine

encephalographic procedure are included.

Case 1. A 50 year old woman was admitted to the psychopathic hospital with a history of mental disturbance of three months' duration. Her symptoms included delusions and headaches. She had withdrawn from society and had attempted suicide once.

Neuropsychiatric examination revealed disjointed and circumstantial speech, defect of recent memory, occasional agitation, intelligence quotient of 89, gross impairment of mental functioning suggestive of organic brain involvement, hyperactive tendon reflexes, and a suggestion of ataxia in the upper extremities. Other physical findings were essentially normal except for blood pressure of 140/96. Roentgenograms of the chest and skull were

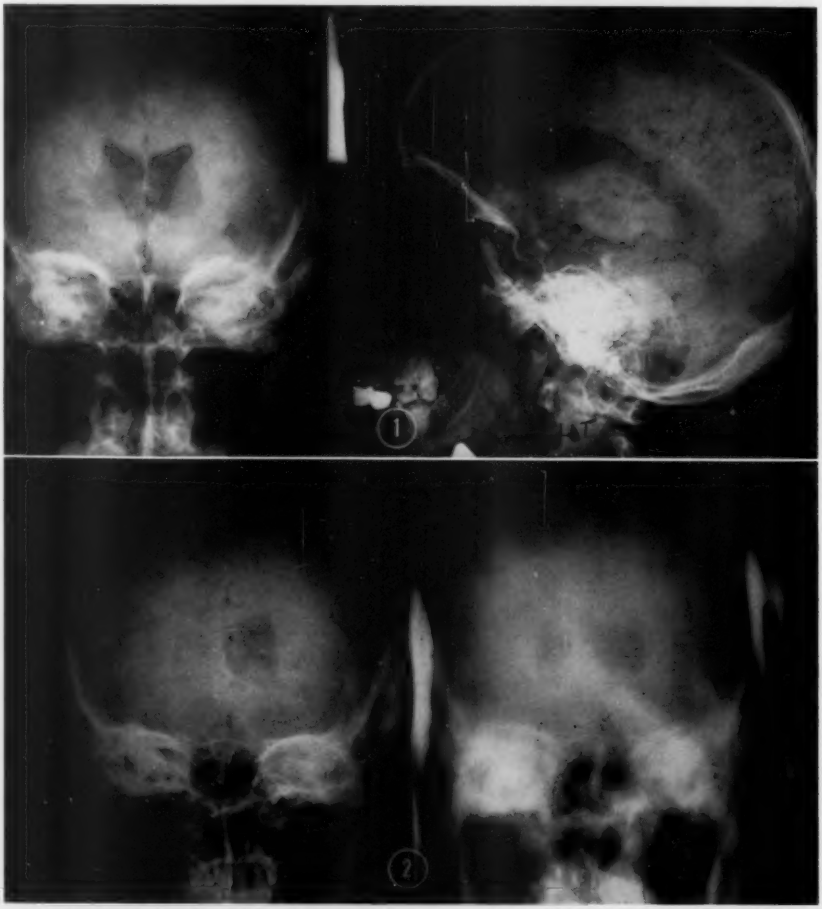


FIG. 1. *Case 1.* Excellent filling of the ventricular system and subarachnoid space is evident. FIG. 2. Two hour serial view (left) indicates considerable absorption of gas; 24 hour serial view (right) shows no further change in amount of gas present.

normal. A lumbar puncture revealed normal cerebrospinal fluid pressure, 2 cells per cu. mm., protein 40 mg. per cent, and sugar 75 mg. per cent.

Pre-encephalographic medication consisted of Nembutal 200 mg. and atropine 0.4 mg. orally. Encephalography was performed with removal of 80 ml. of cerebrospinal fluid and injection of 90 ml. of xenon. The procedure was uneventful. Total postencephalographic medication consisted of aspirin 0.7 gm. given twice during the first 24 hours. There were no unusual complaints. Highest temperature was 100.8° F. rectally on the evening of the procedure.

The encephalograms (figure 1) showed excellent filling of the ventricular system and subarachnoid space; no abnormality was demonstrated. Serial films (figure 2) revealed considerable absorption of gas within the first two-hour period, but no apparent change in the amount of gas during the next 22-hour period.

The patient improved with electroshock therapy beginning the third postencephalographic day.

Case 2. A 52 year old man was admitted to the hospital with a history of recurring blackout spells of six weeks' duration. These episodes were usually associated with coughing. A right pneumonectomy had been performed a year and a half earlier for bronchogenic carcinoma.

Neurologic examination revealed no focal findings. There was some question whether the patient was having bouts of ptussive syncope or seizures due to carcinoma metastatic to the brain.

Pre-encephalographic medication consisted of Seconal 100 mg. orally and Demerol 75 mg. subcutaneously. Encephalography was performed with removal of 65 ml. of cerebrospinal fluid and injection of 65 ml. of xenon. Initial cerebrospinal fluid pressure was 470 mm.; final pressure was 360 mm. The patient complained of weakness and nausea during the procedure and perspired appreciably. Eight hours after the procedure he complained of severe headache as the only residual symptom. Total postencephalographic medication consisted of codeine 60 mg. and aspirin 1.5 gm. given during the first 18 hours. There was no temperature elevation.

The encephalograms (figure 3) showed excellent filling of the lateral and third ventricles and some filling of the subarachnoid spaces. No abnormality was demonstrated. Serial films (figures 4 and 5) revealed marked diminution of gas within the first two-hour period, but no significant change in the subsequent 24-hour period.

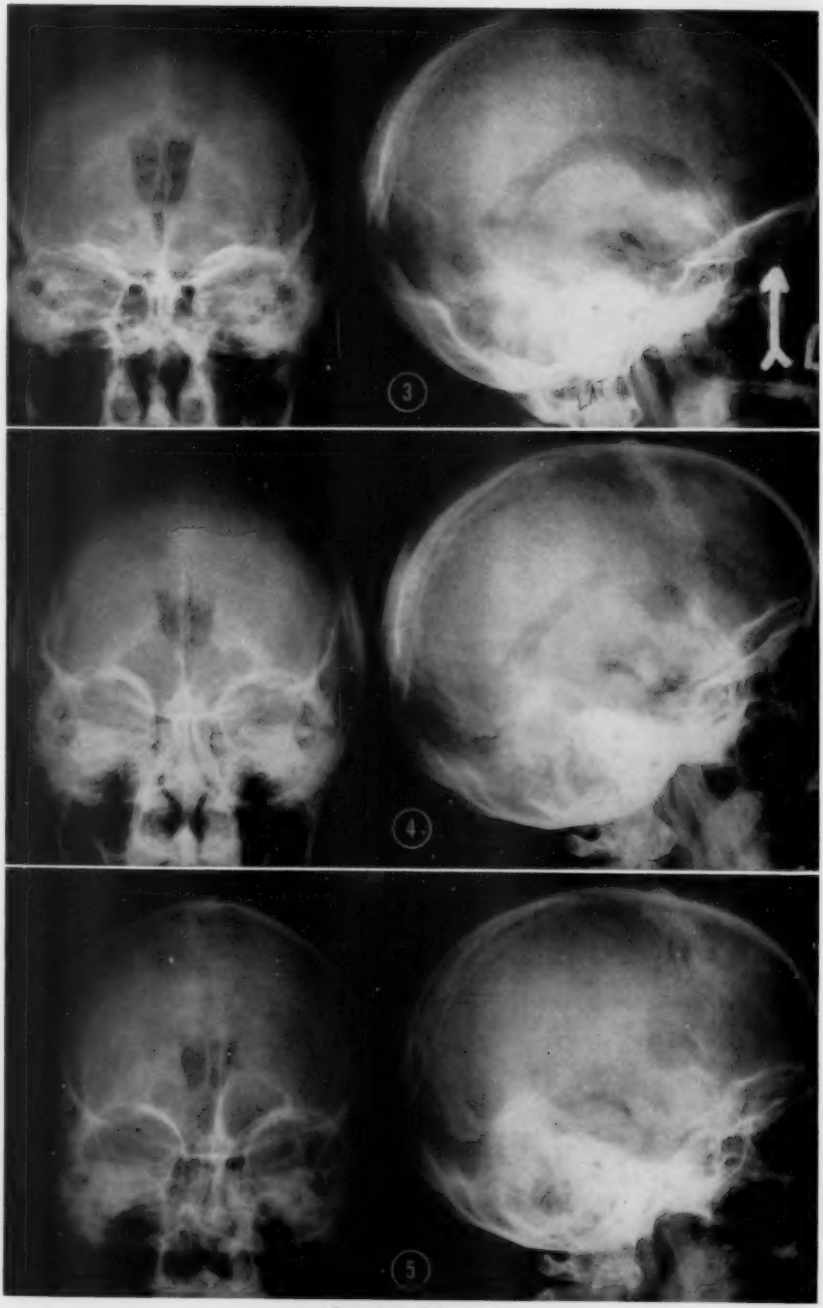
The patient was discharged on anticonvulsant medication. He expired six months later of recurrent bronchogenic carcinoma.

Case 3. A 43 year old woman was admitted to the hospital with a history of increasingly severe headaches during the previous nine months. The headaches were described as severe, throbbing, generalized pain, occasionally accompanied by nausea and vomiting, but generally not preceded by any aura. They were not relieved by the usual analgesics. During the six-day period of hospitalization prior to encephalography, the patient was given aspirin, APC, and Gynergen, with relief obtained only from the latter drug. She also received a sedative each evening to sleep.

The findings of the general physical examination were normal. Neurologic examination revealed subjective diminution of pain sensation over the right fourth and fifth fingers. There was questionable weakness of the triceps on the right side. Routine blood and urine examinations revealed normal findings. Blood serology was negative. A lumber puncture showed an initial pressure of 160 mm. Cerebrospinal fluid was clear and colorless and contained no cells; protein was 44 mg. per cent. Roentgenograms of the skull and chest were normal.

Pre-encephalographic medication consisted of Seconal 200 mg. and Dramamine 50 mg. orally. Encephalography was performed with removal of 65 ml. of cerebrospinal fluid and injection of 65 ml. of xenon. Initial cerebrospinal pressure was 244 mm.; final pressure was 240 mm. The patient complained of severe headache during the latter part of the procedure. She

FIG. 3. *Case 2.* Anteroposterior and lateral views demonstrate excellent visualization of the lateral and third ventricles; a small amount of gas is present in the frontal subarachnoid space.
FIG. 4. Two hour serial views. An apparent diminution in the amount of gas from that apparent in figure 3 is evident.
FIG. 5. Twenty-six hour serial views. There is no apparent significant change from the previous examination, figure 4.



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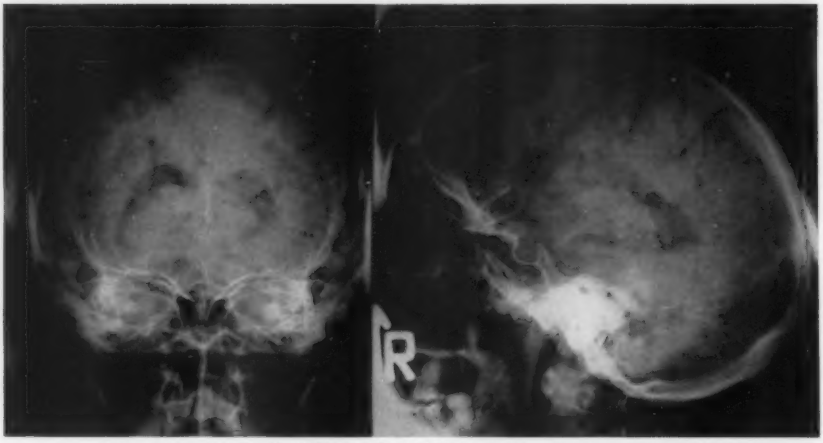


FIG. 6. *Case 3.* Excellent filling of the ventricles and subarachnoid spaces is evident.

had only her usual headache by the morning after the procedure. Total postencephalographic medication consisted of codeine 360 mg., aspirin 3.5 gm., Dramamine 50 mg., Seconal 180 mg., and Gynergen 0.5 mg. given in divided doses upon seven p.r.n. requests during the first 42 hours. Highest temperature was 101.4° F. rectally on the day after the procedure; temperature was normal the next day.

The encephalograms (figure 6) showing excellent filling of ventricles and subarachnoid spaces were interpreted as normal.

The patient was discharged on the second postencephalographic day, stating she was well enough to travel the 200-mile distance to her home by car. The tentative diagnosis was migraine headaches.

Case 4. A 49 year old woman was admitted to the hospital with a history of disturbed sleep patterns extending over a period of about seven years and becoming increasingly troublesome. She was sleeping approximately 22 hours each day, according to her family. She could be aroused easily, but would go back to sleep immediately. She had received Dexedrine and thyroid at various times in the past without noticeable benefit.

The findings of the physical examination were normal except for moderate obesity and minimal residuals of poliomyelitis evident in the left lower extremity. An extensive laboratory examination included studies of protein-bound iodine, blood cholesterol, blood electrolytes, skull and chest roentgenograms, and electroencephalography. All laboratory findings were within normal limits except for the electroencephalograms, which were reported as showing abnormal slow activity from both hemispheres, not typical of that seen in narcolepsy but suggestive of an expanding lesion deep and near the midline.

Pre-encephalographic medication consisted of Seconal 200 mg. and Dramamine 50 mg. orally. Encephalography was performed with removal of 70 ml. of cerebrospinal fluid and injection of 70 ml. of xenon. The procedure was uneventful. Initial cerebrospinal fluid pressure was 360 mm.; final pressure was 240 mm. Total postencephalographic medication for headache consisted of codeine 120 mg. and aspirin 1.5 gm. given in divided doses upon three p.r.n. requests during the first 48 hours. Nausea and vomiting persisted for about three days. There was no temperature elevation.

The encephalograms (figure 7) showed fair visualization of the lateral and third ventricles, and afforded evidence of a rounded elevation projecting into the bodies of the lateral ventricles, suggestive of a tumor in the region of the third ventricle.

Ventriculography was performed six days after the xenon encephalography; again the filling of the ventricular system was not entirely satisfactory, but no distortion of the lat-

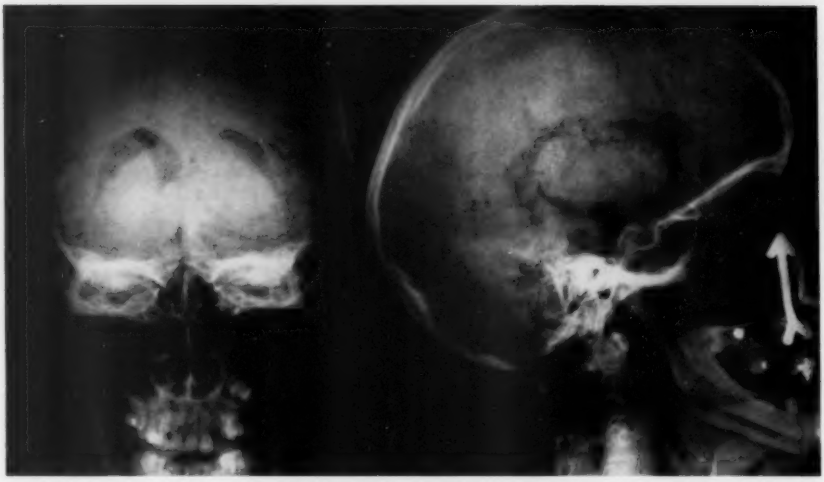


FIG. 7. *Case 4.* Fair visualization of the lateral and third ventricles as well as the incomplete filling of the subarachnoid spaces is shown; the cisterna magna is visualized, as is the upper cervical cord.

eral ventricles was apparent. The patient was discharged after 35 days of hospitalization, during which time she was placed on Dexedrine Spansule medication beginning the day after encephalography. At the time of discharge she was somewhat improved, but there was no well established diagnosis nor etiology.

Case 5. A 38 year old woman was admitted to the hospital with a history of seizures since the age of 12. The seizures, as described by her family physician and as observed by staff members, were undoubtedly psychomotor in character.

The general physical and neurologic examinations revealed no significant abnormality. The laboratory findings and roentgenograms of lungs and chest were within normal limits. An electroencephalogram revealed abnormal focal activity over the left temporal area. Phenurone was quite effective in suppressing seizures but was discontinued because of early signs of toxic hepatitis, and encephalography was decided upon.

Pre-encephalographic medication consisted of Seconal 100 mg. and Dramamine 50 mg. orally. Encephalography was performed with removal of 70 ml. of cerebrospinal fluid and injection of 70 ml. of xenon. The procedure was uneventful except toward the end when the patient complained of feeling cold and she appeared somewhat pale. Initial cerebrospinal pressure was 270 mm.; no final pressure was taken. Total postencephalographic medication for mild headache consisted of codeine 120 mg. and aspirin 1.5 gm. given in divided doses upon two p.r.n. requests within the first 18 hours. Seizures resumed on the first postencephalographic day. Highest temperature was 100.0° F. rectally on the day of the procedure; temperature was normal the next day.

The encephalograms (figure 8) showed satisfactory visualization of the lateral ventricles and subarachnoid spaces, but revealed no abnormality.

The patient was discharged 13 days after encephalography on Mysoline anticonvulsive therapy.

Case 6. A 55 year old man was admitted to the hospital with a history of generalized headaches, beginning in the previous month. The headaches came to be associated with nausea and vomiting and were of increasing intensity. For about ten months prior to admission he had noticed defective depth perception and difficulty with close vision. Just prior to admission he had driven a tractor off the road into a ditch on two occasions, apparently because he was unable to judge distance.

FIG. 8. *Case 5.* Visualization of the lateral ventricles and subarachnoid spaces is good.

The general physical examination was normal. Neurologic examination showed dysdiadokokinesis of the left hand and leg, a loss of the left abdominal reflex, and slightly more active tendon reflexes in the left upper and lower extremities. A lumbar puncture revealed 110 cells (lymphocytes), a quantitative protein of 104 mg. per cent, and a spinal fluid sugar of 25 mg. per cent. Roentgenograms of the skull and chest were within normal limits. The spinal fluid showed a midzone rise on the colloidal gold test.

Pre-encephalographic medication consisted of Seconal 200 mg. and Dramamine 50 mg. orally. Encephalography was performed with removal of 70 ml. of cerebrospinal fluid and injection of 70 ml. of xenon. The patient tolerated the procedure well until 50 ml. of gas had been injected, at which time he retched but did not vomit. He was asleep prior to the beginning of encephalography and was returned to the ward asleep after the procedure. Postencephalographic medication consisted of codeine 120 mg. given in two doses on the day of the procedure. The patient was asymptomatic after the second postencephalographic day. There was no temperature elevation.

The encephalograms (figure 9) showed a satisfactory filling of the left lateral ventricle and subarachnoid spaces, but no filling of the right lateral ventricle. A decrease in the amount of filling was seen two hours after the initial examination (figure 10); a further decrease in filling was evident six hours after the initial examination (figure 11).

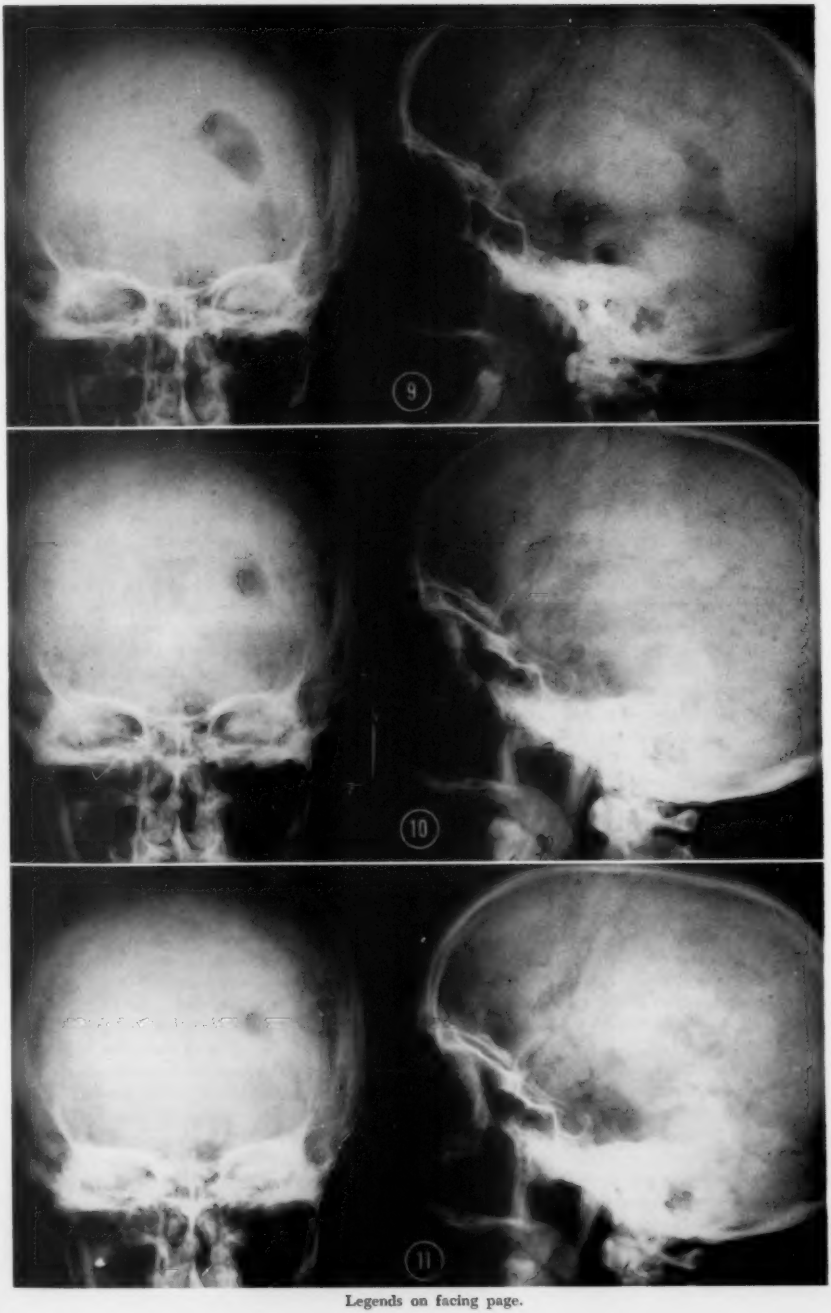
The patient remained asymptomatic after the second postencephalographic day and was discharged on the twelfth postencephalographic day. The diagnosis was virus encephalitis.

Case 7. A 42 year old man was admitted to the hospital with a brief history of severe headache and weakness of the right upper extremity. He was stuporous on admission. Upon examination he was noted to have a purulent infection in the left middle ear and evidence of meningeal inflammation. Ten days after admission a radical mastoidectomy was performed, with transient improvement in alert-

FIG. 9. *Case 6.* There is satisfactory evidence of filling of the left lateral ventricle and subarachnoid spaces but not of the right lateral ventricle.

FIG. 10. Two hour serial views. A decrease in the amount of filling is evident upon comparison with figure 9.

FIG. 11. Six hour serial views. A comparison with figure 10 indicates a further decrease in the amount of filling.



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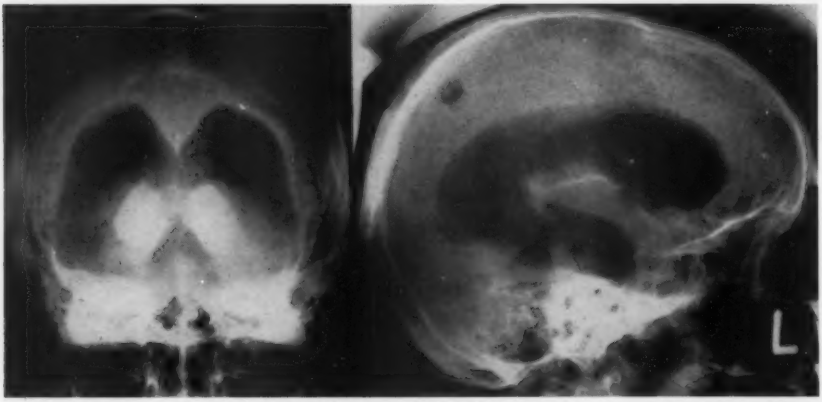

FIG. 12. *Case 7.* There is excellent visualization of the lateral, third, and fourth ventricles but not of the subarachnoid spaces. The dilation of the ventricular system is symmetric.

ness. He continued to be febrile in spite of antibiotics and nine days later he showed a definite depression of consciousness. The mastoidectomy was revised at this time and cholesteatomatous material, left intact during the first operation, was completely removed. There was little improvement after this procedure, and on the third postoperative day angiography was done through both carotid arteries. No significant abnormality was noted. Ventriculograms were done ten days after angiography and these revealed only mild internal hydrocephalus. Following this procedure he was in decerebrate rigidity for several weeks. He eventually showed slight improvement, but a cerebral abscess was still considered a possibility and encephalography was planned.

Pre-encephalographic medication consisted of Seconal 200 mg., Thorazine 25 mg., and Dramamine 50 mg. Encephalography was performed with removal of 200 ml. of cerebrospinal fluid and injection of 160 ml. of xenon and 40 ml. of air. The patient complained of moderate headache during the procedure. There was no nausea or vomiting. He was sufficiently recovered to eat a full meal two hours after the procedure. Total postencephalographic analgesics consisted of codeine 240 mg. given in four q. 4/h doses of 60 mg. each. There may be doubt whether the patient required the medication, since it was noted that he was lethargic for 36 or more hours and awoke only to eat his meals. His temperature rose to 101.0° F. rectally on the day of the procedure and fluctuated between that and normal for two days, after which he remained afebrile.

The encephalograms (figure 12) indicated excellent filling of the lateral third and fourth ventricles but not of the subarachnoid spaces; symmetric dilation of the ventricles was revealed.

There was gradual improvement during the next three months, after which he was discharged to a nursing home for further convalescence. The final diagnosis was meningoencephalitis of nonspecific origin.

Case 8. A 51 year old man was admitted to the hospital with a history of a head injury approximately 48 hours earlier, which was followed by headache. On the day previous to admission he came home from work complaining that he was unable to read, and the next morning his wife was unable to arouse him. When he was examined it was suspected that he was suffering from some form of intoxication. A blood specimen was reported as showing 150 mg. per cent of bromide. On specific questioning the relatives recalled that he had been taking one or more doses of Bromo-Seltzer for a considerable period. The patient denied this. The history accompanying this patient indicated that he had been admitted to a Veterans Administration facility repeatedly for "mental aberrations." On two occasions he had been found to have elevated spinal fluid protein (178 mg. per cent on one occasion, and 182 mg. per cent on another). Electroenceph-

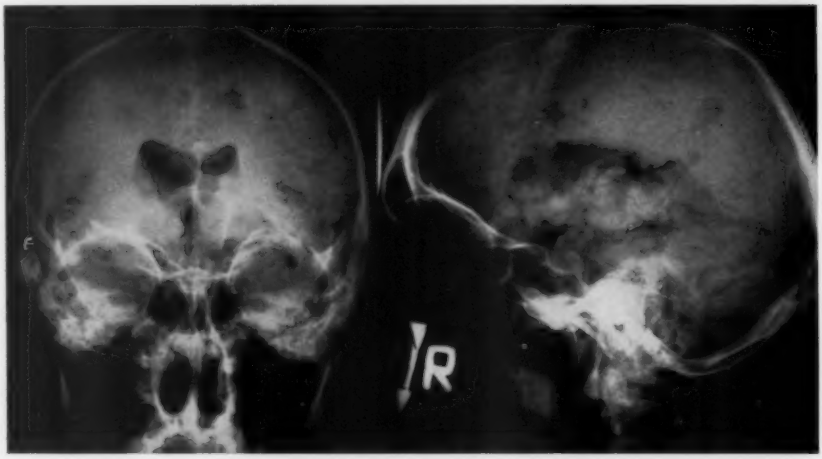

FIG. 13. *Case 8.* There is satisfactory visualization of the lateral and third ventricles. The subarachnoid spaces are incompletely filled, but dilatation is evident in some of them.

alograms had been abnormal on several occasions. A pneumoencephalogram three years before admission was reported as showing a dilated right lateral ventricle.

The physical findings were within normal limits, except that blood pressures obtained several times during the first few days of hospitalization were about 180/110. A lumbar puncture on the day of admission revealed an initial pressure of 220 mm. The fluid was clear and colorless, and contained 1 white cell per cu. mm. and a total protein of 100 mg. per cent. Blood and spinal fluid serologies were negative. Roentgenograms of the skull and chest were normal. An electroencephalogram showed diffusely abnormal slow activity. Encephalography was done 13 days after admission.

Pre-encephalographic medication consisted of Seconal 200 mg. and Dramamine 50 mg. orally. Encephalography was performed with removal of 176 ml. of cerebrospinal fluid and injection of 187 ml. of xenon. During the procedure the patient complained of severe headache, was cool, perspired freely, and vomited once. The blood pressure remained stable at approximately 150/80. Total postencephalographic medication consisted of codeine 60 mg. and two tablets of APC, all given within the first 17 hours. On the morning after the procedure the headache and nausea had disappeared. Highest temperature elevation was 101.2° F. rectally on the day after the procedure; temperature was normal thereafter.

The encephalograms (figure 13) visualized the ventricles and subarachnoid spaces satisfactorily. A diffuse cortical atrophy, more marked on the right, was indicated. The patient was discharged 11 days after the procedure.

Case 9. A 48 year old man was admitted to the hospital with a history of headaches, amnesia associated with a brief loss of consciousness but no convulsion, and a disturbance of control of the left-sided extremities, along with some sensory loss on that side. These symptoms developed during the two weeks prior to admission. There was a history of a somewhat similar episode one year earlier. He had been thought to have a slight residual weakness of the right leg.

The general physical examination revealed a normal man with blood pressure 108/65. The neurologic examination revealed a generalized hypesthesia on the left side, slowed alternating motion rate in the left extremities, and a diminution of strength on that side to approximately 90 per cent of normal. Routine blood and urine examinations were within normal limits. Blood and spinal fluid serologies

were negative. Roentgenograms of the skull and chest were negative. Visual fields were within normal limits. A lumbar puncture in another hospital, just prior to this admission, revealed an initial spinal fluid pressure of 65 mm., with a total protein of 31 mg. per cent and sugar of 75 mg. per cent. There were only 2 leukocytes in the spinal fluid. The electroencephalogram was within normal limits.

Pre-encephalographic medication consisted of Seconal 200 mg. and Dramamine 50 mg. orally. Encephalography was performed with removal of 100 ml. of cerebrospinal fluid and injection of 100 ml. of xenon. The patient noted only mild headache and no evidence of nausea or other discomfort during the procedure. Post-encephalographic medication consisted of codeine 60 mg. given on two occasions within the first eight hours. The headache cleared completely within 24 hours. Highest temperature was 100.6° F. rectally on the day of the procedure; temperature returned to normal the next day.

The encephalograms (figure 14) showed excellent filling of the subarachnoid spaces but only of the right lateral ventricle, particularly the atrium and occipital horn. Some cerebral atrophy was apparent. Serial films (figures 15 and 16) revealed considerable absorption of gas within the first two-hour period and evidence of further absorption in the subsequent four-hour period.

The patient was discharged 12 days after the procedure with a diagnosis of cerebral atrophy due to vascular disease.

Case 10. A 58 year old man was admitted to the hospital because of "spells" which had their onset almost four years previously. He had been given various medications which did not control the seizures adequately. During the year prior to admission he was noted to have some disturbance of use of the left arm and leg; he was also bothered by frequently recurring headaches. He noticed after one of his spells that his tongue was bitten and bleeding. From the wife's description there can be little doubt he had generalized convulsive seizures.

The physical findings indicated mild left hemiparesis, right ulnar palsy of undetermined etiology, and generalized atherosclerosis. Because of the history of progressive involvement and the left hemiparesis, it was felt that a right-sided brain tumor was a possibility.

Pre-encephalographic medication consisted of Seconal 100 mg. and Thorazine 25 mg. Encephalography was performed with removal of 60 ml. of cerebrospinal fluid and injection of 55 ml. of xenon. The patient had remarkably little headache and no nausea during the procedure and immediately afterward. The only postencephalographic distress was a very mild headache the next day. No medication was required. Highest temperature was 101.4° F. rectally on the day of the procedure; temperature returned to normal within 24 hours.

The encephalograms (figure 17) demonstrated excellent visualization of the ventricular system and the subarachnoid spaces. No abnormality was detected. Figure 18 indicated a considerable decrease in the amount of gas present after 24 hours.

The patient was started on Dilantin 100 mg. three times daily and discharged on the second day after the procedure.

DISCUSSION

Roentgenographic results obtained during xenon encephalography were comparable in quality to those obtainable under similar conditions with injections of air.

Serial follow-up films made in half of the cases indicated a marked diminution in the visible gas during the first two-hour period after injection. A progressively slower diminution in the amount of residual gas was evident during the subsequent two- to four-hour period. The residual gas present 24 hours after xenon injection was not appreciably less than that six hours after injection. The rapid diminution of ventricular gas after

FIG. 14. *Case 9.* Excellent filling of the subarachnoid spaces but evident only in the right lateral horn. Some cerebral atrophy is apparent.

FIG. 15. Two hour serial views. A marked diminution in the apparent amount of gas filling the ventricle and subarachnoid spaces is evident upon comparison with figure 14.

FIG. 16. Six hour serial views. A comparison with figure 15 indicates further diminution in the amount of residual gas.

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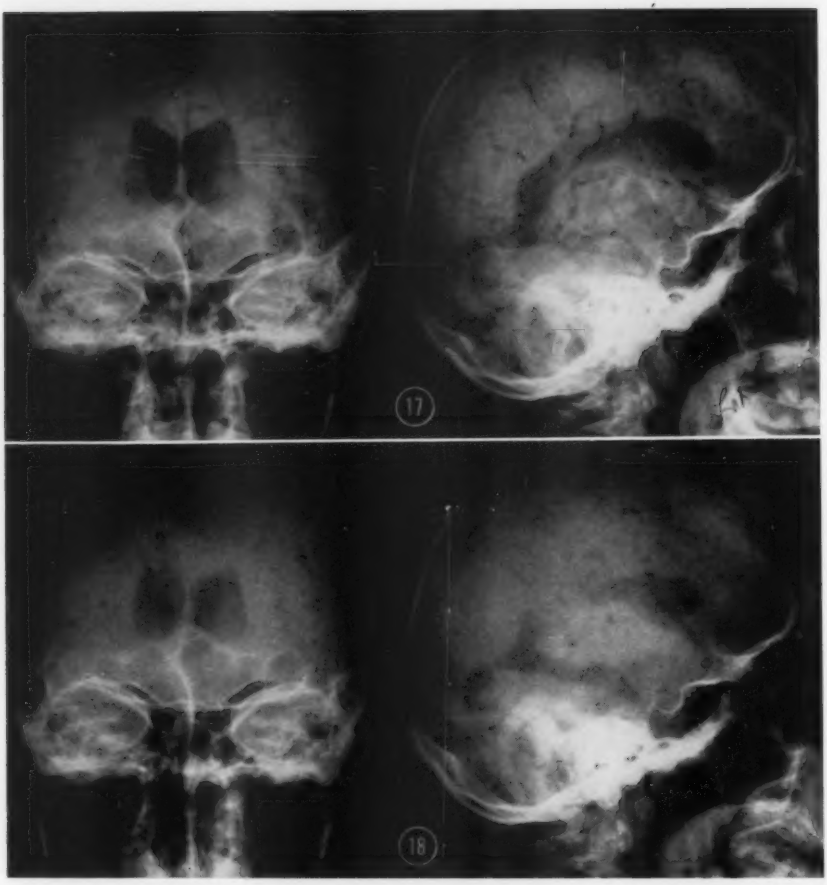

FIG. 17. *Case 10.* There is excellent visualization of the ventricular system and subarachnoid spaces. No abnormality is evident.
FIG. 18. Twenty-four hour serial views. Comparison with figure 17 indicates an appreciable reduction in the apparent amount of residual gas.

xenon injection was probably the result of its rapid diffusion into the blood stream and elimination from the lungs. The residual gas after this period of rapid diminution was probably a mixture of blood gases, mostly nitrogen and oxygen, which had diffused into the ventricles.

There was no clinical evidence of sedation, hypnosis, or respiratory depression associated with xenon encephalography. Neither was there any suggestion of greater or lesser distress during the xenon encephalographic procedures than during ordinary pneumoencephalography.

Any benefits resulting from the substitution of xenon for air in encephalography are probably associated with the postencephalographic period. To determine the effect of xenon substitution for air upon the incidence, degree, and duration of postencephalographic distress, a controlled, comparative study involving large series of cases with xenon and air is necessary. Justification for the routine use of xenon in encephalography will be dependent upon the demonstration of an appreciable and significant decrease of postencephalographic morbidity.

CONCLUSIONS

The quality of roentgenographic results obtained during xenon encephalography was comparable to that obtainable by subarachnoid air injections.

Residual ventricular gas rapidly diminished in quantity during the first several hours after the injection of xenon.

Xenon encephalography produced no evidence of sedation, hypnosis, or respiratory depression during or after the procedure.

Xenon used in this study was furnished by Linde Air Products, Inc.

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■ From the facts we have related, concerning voluntary movements, we think it may be concluded that the idea that there are two columns of the spinal cord (the anterior) alone employed in the production of these movements, must be completely abandoned. It is extremely probable that the voluntary motor conductors pass in the anterior pyramids, and, after having made their decussation, pass chiefly in the lateral columns of the spinal cord and in the gray matter near these columns, and, at last, that, after a short distance, a number of these conductors leave the lateral columns to pass into the gray matter and into the anterior columns.

CASE REPORT

Prolonged Alterations in Behavior Associated with a Continuous Electroencephalographic (Spike and Dome) Abnormality

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ALTERATIONS in the sensorium varying from mental confusion to unconsciousness are characteristic of convulsive disorders. However, these alterations are usually paroxysmal and of short duration, lasting from seconds to a few minutes or even two to three hours. When the mental changes persist for longer periods, it becomes questionable whether the altered behavior is a paroxysmal disorder.

The following report presents a patient whose prolonged mental disturbance coincided with an abnormal electroencephalographic pattern consisting of almost continuous three to four cycles per second spike and dome waves.

CASE PRESENTATION

A 19 year old college girl was admitted to Mount Sinai Hospital on August 20, 1954 with the chief complaint of persistent mental confusion of about eight hours' duration.

The patient was apparently in good health until about the age of 13 (1948) when, with menarche, there began short spells of "absence or staring, as if she were dreaming or away somewhere." These episodes were brief and might occur once or twice daily, varying in frequency according to the time of month (most frequent during menstruation) and the patient's emotional state. No major seizure phenomena were ever noted.

On October 20, 1950 the patient became incoherent, confused, disoriented, and "hazy." She spoke irrelevantly and seemed to confabulate. Coincidentally, the patient complained of a stiff neck and had a slight fever. The following day she was seen by a neurologist whose examination revealed no abnormalities other than some pain on deviation of the head to the left. There were no symptoms during the next three days. A lumbar puncture revealed crystal clear and colorless cerebrospinal fluid under an initial pressure of 170 mm. of water. It contained two cells and a total protein of 41 mg. per cent. An electroencephalogram was reported as normal.

She was seen again in March 1951, at which time there were no complaints and the neurologic examination revealed no abnormality. In the intervening period there had been as many as ten momentary lapses of consciousness daily.

In December 1951 she was found wandering "lost" in the high school she attended. She was disoriented and spoke incoherently. This state lasted two days. Afterward she resumed her previous activities with a complete amnesia for the incident.

On January 28, 1954, after having completed a philosophy examination at the University of Michigan, she returned to her room and began playing cards. She suddenly got up, walked out without a coat, went to the airport, and boarded a plane to New York without a ticket. Upon arrival in New York she was charged as a stowaway. She was found to be confused and incoherent. When seen the following day by the same neurologist as in March, she was again normal.

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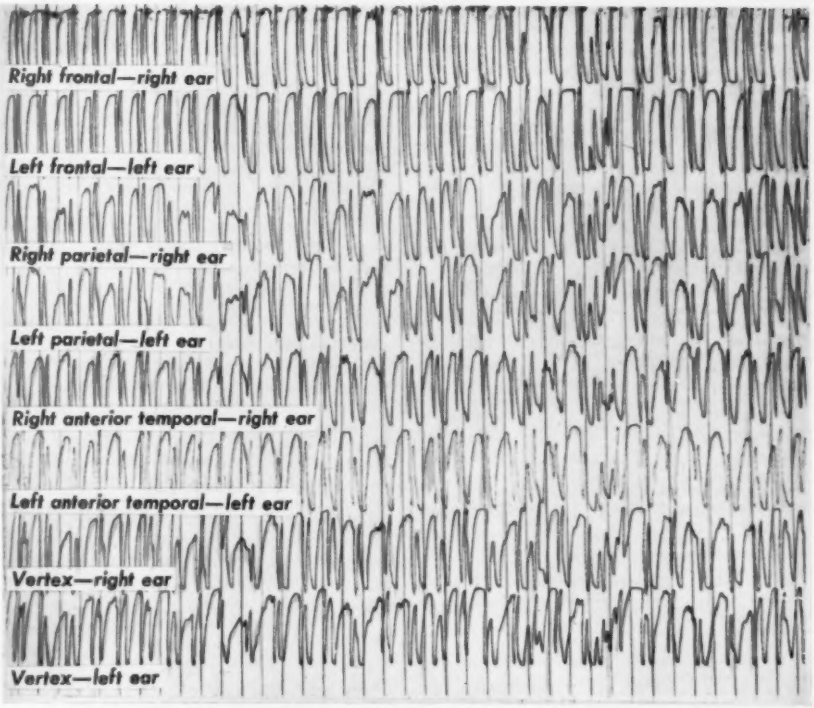

FIG. 1. Ten second record of the electroencephalographic abnormality; this pattern was present without interruption for a period of hours.

On August 20, 1954 at 9:30 a.m., while working at her father's office, she suddenly became confused, incoherent, and forgetful. The behavioral changes persisted. She was examined some six hours later. The neurologic status at this time revealed disorientation for time and place, misnaming of objects, right-left disorientation, and inability to calculate simple sums. There were bizarre errors with displacements in the face-hand test. Ishihara plates were read correctly. In spite of these changes she appeared alert, was cooperative in her performance, and showed good affect. The remainder of the neurologic examination was normal.

Many of the findings were suggestive of hysterical behavior, especially when her answers were approximately correct (Ganzer syndrome). All of the episodes of altered behavior were reported as having been associated with emotional tension or menstruation. Each of the three previous disturbances lasted for many hours.

An electroencephalogram revealed a grossly abnormal record in all leads. This was characterized by continuous three to four cycles per second spike and dome patterns.

She was referred to Mount Sinai Hospital for further studies. General physical examination was entirely within normal limits except for continuous fluttering of the closed eyelids at a rate of three to four per second. The patient's temperature was 98° F, pulse 80, respirations 20, blood pressure 110/76. The blood count was normal and the fasting blood sugar 86 mg. percent. A casual urine specimen had 1 plus albumin and contained many red blood cells (patient was menstruating).

Neurologic examination revealed the patient to be apparently alert and cooperative. Examination of the cranial nerves, sensorimotor

status, and deep tendon reflexes revealed no abnormalities. However, she was disoriented for time and place, mentally confused, revealed gross memory impairment for both recent and past events, calculated with marked difficulty and many errors, perseverated, and executed poorly commands requiring crossing the midline. There was no aphasia. The face-hand test was normal. There was no alteration in affect and no delusions or hallucinations. On several occasions she manifested the syndrome of approximate answers (Ganzer syndrome).

Some of the characteristic responses to questioning were as follows:

What date is it? Nov. 19, 1935 (her birthdate).
How old are you? I'll be 16 Nov. 15, 1954.
What date is it? Nov. 15, 1954.
Where are you? The Harkness Pavilion (Mt. Sinai Hospital, Guggenheim Pavilion).
What is the address? 100th St. and 100th Ave.
Where are you now? My father's office.
What day is this (Friday)? Tuesday, Sunday.
How much is 6 plus 8? 14.
9 minus 4? 16.
3 times 4? 16.
How old are you? 16.
What do you do? I'm a model.
Who is the president of the U.S.? Churchill.
What is the capital of the U.S.? I don't know.
What is the capital of Italy? Venice.
Where were you this morning? Women's Hospital, 16th floor.
What is the date? Nov. 16, 1935.
Is this 1935? No, 1954.
Where are you now? South Chester County.
How old are you? I'll be 19.
What do you do? I work for my father, a book-binder.
Do you go to school? I try at Northern, Lord, I can't remember.
How old are you? I'll be 15 on Nov. 15th.

When the patient was pressed and informed about the errors and the possibility of simulation, she became silent or at other times cried.

When asked to draw a house, she drew a box and thereafter perseverated the response when asked to draw a man, a woman, and a tree. She appeared to have much difficulty, erasing and redrawing the lines numerous times. She identified and labeled different parts of the box, however, as the head, arms, and so on.

Electroencephalogram. At about 6 p.m. the patient was examined electroencephalographically. The tracing revealed the identical abnormality which was recorded earlier in the day (figure 1). This consisted of continuous regular high voltage (140 mv.) 3 to 4 cps. spike and wave activity, with single and multiple fast spikes diffuse and bisynchronous. There were occasional 8 cps. waves of 140 mv. recorded posteriorly. The abnormality was recorded for more than three hours, during which time the effects of various external stimuli and drugs were noted. There was no period of normal activity except following the injection of sodium Amytal. An intravenous injection of 50 cc. of a 25 per cent solution of glucose produced no change. Photic stimulation through a range of frequencies from 1 to 30 cps. with the eyes open and closed produced no change.

Intravenous sodium Amytal was injected in a 5 per cent solution at a rate of about 50 mg. per minute to a total of 500 mg. After about 400 mg. had been injected, short bursts of "normal" record occurred. This consisted of 17 to 25 cps. waves of from 20 to 100 mv. The injection was continued until the total dose was given. During this time and for about eight subsequent minutes, the intervening "normal" periods became more lasting and the previously noted abnormality occurred in shorter and shorter bursts. This was true of all leads simultaneously. Finally, about ten minutes after the injection, the spontaneous record was free of abnormality. Any stimulus, however, such as noise, calling the patient's name, pinprick, produced a short burst of the previous pattern. Although the patient was drowsy at this time, she could be aroused easily and responded correctly to questioning. After about 35 minutes the abnormality began to reappear spontaneously in short bursts. The reverse order of events occurred, the bursts becoming longer and the normal record shorter until the 3 to 4 cps. spike and wave forms were again present continuously.

The following morning, or about 24 hours after onset of this episode, the patient's mental status was entirely normal. She was oriented as to time, place, and person, calculated correctly, was able to cross the midline on command such as place your left hand on your right ear, and drew appropriate images of a house, woman, man, and tree. An electroencephalogram revealed a normal resting record which differed from the Amytal record in somewhat slower waves (12 to 18 cps.) of lower voltage (20 to 50 mv.). During hyperventilation several bisynchronous bursts of high voltage spike and wave activity occurred. A similar clinical and electroencephalographic examination was recorded on the third hospital day. The patient was then discharged and has had no recurrence of her difficulty.

DISCUSSION

The terms "prolonged petit mal"[1] and "status epilepticus in petit mal"[2,3] have been suggested to describe prolonged alterations in the state of consciousness associated with more or less persistent spike and slow wave abnormalities in the electroencephalogram. (All of the previously report-

ed patients had had some form of major seizure.)

Of the two cases described by Tucker and Forster,[2] one had experienced "grogginess, confusion, and inability to concentrate" for several days preceding grand mal attacks. Sometimes the major seizure did not ensue. During a 36-hour period of the confused state, bilaterally synchronous 3 cps. spike and wave discharges were noted in long bursts occupying 17 of the 20 minutes of the tracing. The other patient was found "confused, wandering about in a hesitant manner, answering only fragments of questions" one week after having been placed on Dilantin. The electroencephalogram is stated to have shown synchronous 3 cps. spike and wave patterns occurring in long runs with only short intervening bursts of normal electrical activity.

The patient described by Vizioli and Magliocco[1] reported petit mal of increased duration since the onset of grand mal seizures. The petit mal lasted from 15 minutes to over an hour, with many episodes of "automatic states." The published electroencephalographic tracing showed a short burst of spike and wave patterns lasting about three minutes during a period of hyperventilation.

The case most similar to the present one is that published by Schwab.[3] The patient described "peculiar states of mind," "a daze" lasting from one to two days. When examined she was noted to stare and blink her eyes and seemed to be having one seizure after another. Between spells the patient responded to simple commands, but could not answer questions intelligently, offered no spontaneous conversation, and appeared like a person under heavy sedation with the state of consciousness severely obtunded. Over two hours of electroencephalographic recording was characterized by a series of spike and wave patterns with only a second or two between each.

The barbiturates have been reported as less active than the oxazolidine-2, 4-dione derivatives in idiopathic epilepsy. However, Lennox, Gibbs, and Gibbs[4] demonstrated that sodium phenobarbital given to patients with petit mal was effective in prolonging the interval between seizure patterns, which themselves became short and distorted. In a study of patients with organic disease of the brain, Bergman, Stroo, and Feinstein[5] noted that intravenous sodium Amytal produced a reduction or disappearance of previously present slow activity in the records of 21 patients whose spontaneous records were abnormal. In these patients, as well as in those with or without organic brain disease whose electroencephalograms were normal, intravenous sodium Amytal produced a diffuse, symmetric fast activity (15 to 25 cps.). This effect has been reported previously for sodium Amytal by Cohn and Katzenelbogen[6] and Rubin, Malamud, and Hope,[7] and for sodium Amytal, sodium Pentothal, and sodium pentobarbital by Brazier and Finesinger.[8] The latter authors observed fast waves appearing in various parts of the cortex at different times, first in the frontal lead, then the parietal, and finally the occipital. Recovery occurred in the opposite direction.

The present patient demonstrated all these features except the temporal difference in the various electroencephalographic leads. Although the abnormality could be provoked in the electroencephalogram while the patient was influenced by Amytal, her responses to questioning during this period were normal. Thus, one might say that the provoked discharges were subclinical.

In their discussion of a number of varieties of interference with normal intellectual and emotional functions in a presentation of "dullness as an epileptic equivalent," Putnam and Merritt[9] stress the importance of the electroencephalogram as the most objective differentiating tool. The present case is another illustration of the usefulness of the electroencephalogram in differentiating an organic from a psychogenic disorder. The anamnestic relationship of the major episodes to periods of emotional stress and the lack of any history of other previous

convulsive phenomena, even after the electroencephalographic tracings had been seen, posed an impossible differentiation on clinical grounds alone. It must be kept in mind, however, that there are instances of transient impairment of mental states and consciousness which are not associated with electroencephalographic changes. The lack of electroencephalographic abnormalities does not, however, exclude the possible organicity of the disorder.

SUMMARY

1. The case is presented of a 19 year old girl in whom a prolonged and severe defect in mental performance was associated with continuous electroencephalographic abnormality consisting predominantly of a spike and dome pattern.

2. The abnormal behavior and the electroencephalographic patterns were temporarily abolished by intravenous sodium Amytal.

3. The differential diagnosis between an organic and a functional (hysterical) etiology was resolved largely by the electroencephalogram.

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■ As regards the cerebellum, we find sensibility persisting in the celebrated case of absence of this organ, recorded by Combette. There was also conservation of sensibility in two other cases in which the cerebellum had been totally destroyed by suppuration; at least it is stated that there was no paralysis and no other trouble in the functions of animal life. One of these cases having been considered as impossible by Bouilaud, who read a report about it, at the Académie de Médecine of Paris in 1834, Marc, the learned physician of Louis Philippe, rose and said that it was possible, as he had seen an exactly similar case at the Charité.

C. E. Brown-Séquard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

CASE REPORT

Intramedullary Lipoma of the Spinal Cord

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Lipomas of the nervous system are very rare. When present in the central nervous system, as for example in the base of the brain,[1] around the optic chiasm, third ventricle,[2] mamillary bodies,[3] and posterior perforated space, they do not produce specific symptomatology which would reveal their histologic nature prior to operation or necropsy. In the spinal cord the incidence of lipomas is relatively more frequent, and in general they are associated with congenital malformations such as spina bifida,[4] Klippel-Feil syndrome,[5,6] and ivory vertebra.[7] Spinal cord lipomas constitute 1 per cent of all kinds of tumors. They have a tendency to appear in three stages of life,[8] infancy, puberty, and adulthood (30 to 40 years), and seem to have a predilection for the inferior portion of the cervical or upper thoracic segments of the cord. This does not include the lipomeningocele, which is much more frequent and is often found below the level of the spinal cord.

Corneil and Mosinger[9] classify lipomas of the spinal cord as:

1. Extramedullary
   a. lipomas
   b. angiolipomas
   c. myxolipomas
   d. embryonic lipomas
2. Intramedullary
   a. lipomas associated with congenital anomalies
   b. lipomas attached to the pia
   c. intradural lipomas in the filum terminale
   d. liposarcomas
   e. myolipomas

In general, these tumors are composed of fatty tissues well differentiated and histologically similar to the adipose tissues found in any other part of the body. Their cells are large and distended with fat, with the nucleus displaced toward the periphery of the cell. Sometimes these adipose masses can be found associated with fibrous tissue — fibrolipomas, hemangiomas (hemangiolipomas)[5] — or with muscle fibers (myolipomas).[10]

These tumors could be displacements, inclusions, or embryonic nests of the neural tube occurring during formation of the central nervous system.[2] Bostroem[11] believed that lipomas might be maldevelopments by a process of metaplasia perhaps of ectodermal inclusions. Virchow's[12] theory was that lipomas arise from adult fat cells which on rare occasions are found in the pia. Stookey[13] added other theories of his own and from the work of others. At the present time no theory is universally accepted.

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In a survey made in 1945 Ehni and Love[14] found 29 well established cases, and in only one out of five could the tumor be removed. Johnson[15] gathered eight more cases, of which two had been reported by Asenjo, Contreras, and Espinosa.[16] Tamiguehi and Mufson[8] reported one tumor not removable, and Crosby, Wagner, and Nichols[17] reported another removable tumor.

If any syndrome of an intradural lipoma can be described, it would typically occur in an individual with other congenital anomalies and include a long history of symptoms (mean four years) often dating from childhood, including ataxia, paucity of root pains, lack of spinal fluid block until very late in spite of the large size of the tumor, and widening of the spinal canal radiographically. The following case is illustrative of this syndrome.

CASE REPORT

A 16 year old Negress was admitted to the Cleveland City Hospital on December 13, 1952 because of inability to walk for one day. She dated the onset of her present illness to July 1952 when she jumped off a porch, after which she experienced low back pain and stiffness of the legs for two days. However, a more searching review of her past history revealed clumsiness of the legs which dated from early childhood.

She was seen in the medical outpatient department periodically because of thoracic spine tenderness, which was described as being over T4 and T7. The patient said that coughing was associated with severe pain which localized to the same area. The patient had had back pain about six years previously and was told that she had been sleeping on a mattress that was too soft.

Slow progression of stiffness of both lower extremities occurred over the next six months. By early October the legs were becoming numb and she had to look where she was going to control her feet. She also began falling if she did not support herself. About the same time she had sensations of a full bladder, but was unable to urinate. Occasionally she had episodes of enuresis without any sensation of urinating. She had had no bowel movements for several days prior to admission, but was not aware of any anal sphincter disturbance. A complicating factor was six-month pregnancy at the time of admission.

Physical examination disclosed blood pressure 160/70, pulse 110, respirations 24, and temperature 37.9° C. General physical examination was normal except for a soft blowing systolic murmur at the apex.

Neurologic examination disclosed slight but definite weakness in all muscle groups in both lower extremities. There was some increase in muscle tone to passive motion. Sensory loss to pain sensation extended to the nipple line bilaterally (T5). The patient had no position sense preserved in the lower extremities. The Romberg test was positive and her gait was ataxic. Deep tendon reflexes in the lower extremities were markedly hyperactive, with bilateral patellar and ankle clonus and Babinski signs. The superficial abdominal reflexes were said to be present.

Blood and urine studies were normal, including negative blood serology. Lumbar puncture on December 14, 1952 revealed an initial pressure of 190 mm. of water, crystal clear fluid containing 4 monocytes, and a 4 plus Pandy reaction. The Queckenstedt test was normal. Cerebrospinal fluid chemistries revealed 840 mg. per cent protein and 115.8 mEq. chlorides.

A myelogram done on December 18, 1952 revealed a complete block at T4. The roentgenogram was interpreted as showing an extramedullary lesion, probably a meningioma.

On the following day a laminectomy was performed from T3 to T5, and on opening the dura a large yellow mass protruded into the opening. The capsule of this mass, which was thought possibly to be arachnoid, was opened in an attempt to strip the soft jelly-looking tissue off and get down to the cord, but this ended in failure and the operation was terminated with the dura left open.

Postoperatively the patient began to have pain while passing urine on January 5, 1953 and she had bilateral mass reflexes. By January 13, 1953 she started to have some voluntary movements in the lower extremities. On January 16, 1953 she delivered spontaneously a nonviable fetus. On February 1, 1953 she had her first voluntary bowel movement and felt sensation about the rectum. Power in the left lower extremity showed no improvement. Bilateral hyperactive deep tendon reflexes remained and bilateral mass reflexes developed in the lower extremities. On February 2, 1953 she was reoperated from C5 to T6 to establish the extent of this tumor in order to remove it if possible. This proved to be technically impossible and again the wound was closed. By February 5, 1953 both legs were flexed, and on February 9, 1953 sensation had returned to almost normal in the right lower extremity,

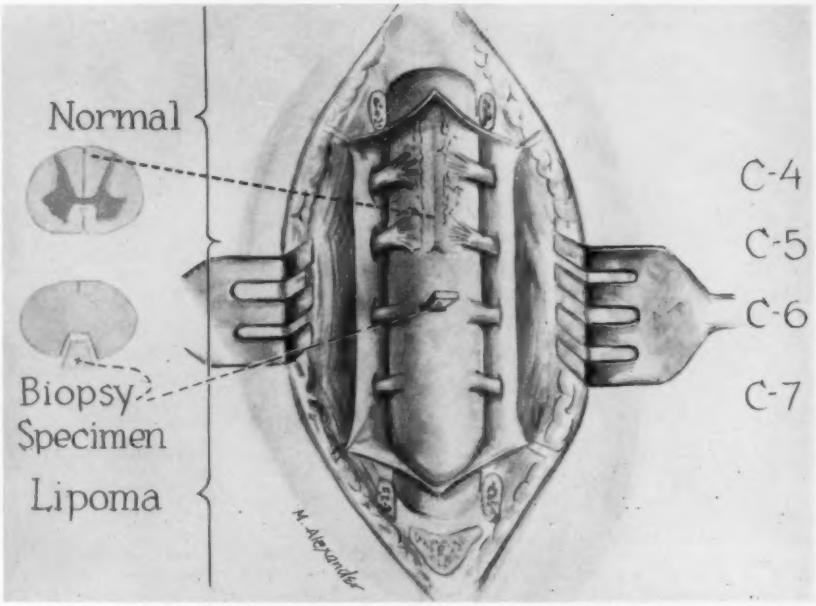

FIG. 1. Diagrammatic sketch of operative findings, showing the sudden obliteration of normal landmarks at the beginning of the tumor tissue and demonstrating the site of the cord biopsy.

where it was completely analgesic prior to the last operation. Very slight movement was also present in the right leg, and she was able to start walking with a walker. The right lower extremity was spastic and much weaker than the left side, which had recovered to a great extent. Bilateral ankle clonus and Babinski signs were present.

On July 28, 1953, she lost motor power in the left lower extremity and experienced sensory loss on the right to about T6-7. She also noted pain and numbness in the upper extremities. Over the period of a month she became incontinent of bladder and bowels. With the impression that this lipoma might be growing slowly upward and that further decompression might be in order, re-exploration was done on November 6, 1953. According to Crosby, Wagner, and Nichols,[17] all of the so-called intramedullary spinal cord lipomas are actually extrapial and can be removed. Attempts were made to free the lipoma from the spinal cord and to establish whether or not this was extrapial. Along the lateral margins of the dural sac the nerve roots could be seen streaming out of the cord, but the tumor tissue was definitely intrapial and could not be removed (figure 1). Inasmuch as she already had paraplegia and weakness of the lower roots of the upper extremity, an attempt was made to remove some of the deeper lipomatous tissue and posterior tracts for analysis of the anatomic relationship of the tumor and spinal cord (figure 2).

Postoperatively the patient continued to complain of neck pain and pain in the ulnar aspect of the upper extremities. There was also some pain in the right shoulder and numbness and tingling in the upper extremities. Postoperatively 4,000 r of roentgen therapy were given in a further attempt to halt the growth of this tumor.

Subsequently an anterior rhizotomy was done in October 1954 to relieve mass reflexes. The patient has been fitted with braces and is in the process of being rehabilitated.

SUMMARY

The case is reported of a 17 year old colored female, who had suffered from spina bifida deformity. In the course of ten weeks following a fall, she developed signs of compression of the upper thoracic spinal cord which rapidly progressed to

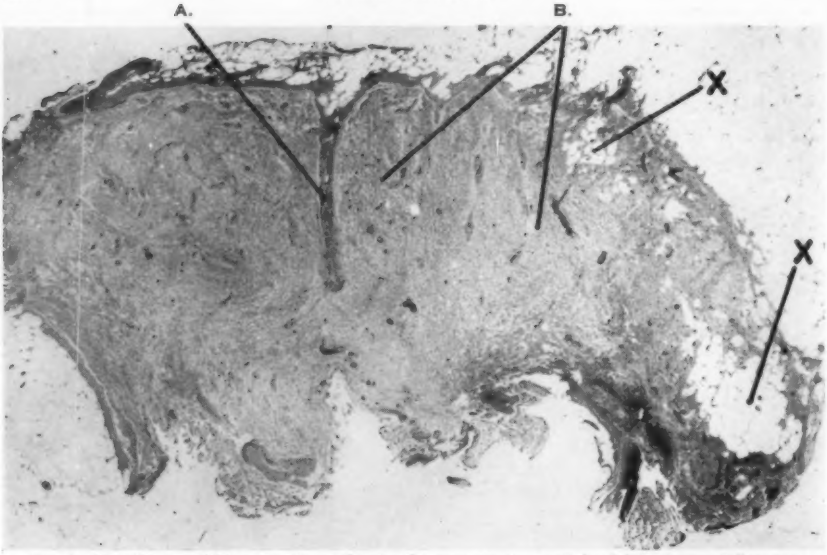

FIG. 2. Magnification of biopsy specimen, showing the gross structure and the definite intramedullary site of part of the lipomatous tissue. *A*. Posterior median sulcus and septum. *B*. Posterior fasciculi. *X*. Intramedullary lipoma.

paraplegia. Laminectomy disclosed an intradural lipoma, a small part of which was removed. Both gross and microscopic examination confirmed the true intramedullary position of this tumor.

We agree with Stookey[14] that most of the intradural lipomas are both intramedullary and extramedullary, with no sharp line of demarcation separating tumor from spinal cord. When such is the case heroic efforts to effect removal would prove too costly from a neurologic standpoint, and splitting of the pia arachnoid and leaving the dura open is the treatment of choice.

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Neurology

BOOK REVIEWS

Brain Mechanisms and Consciousness

A Symposium Organized by the Council for International Organizations of Medical Sciences Established Under the Joint Auspices of UNESCO and WHO. Consulting Editors: Edgar D. Adrian (U.K.), Frederic Bremer (Belgium), Herbert H. Jasper (Canada). Editor for the Council: J. F. Delafresnaye (France). 1954. Springfield, Illinois: Charles C Thomas, Publisher. 556 pages. $8.50.

THIS is the type of book that stirs the reader to intellectual vigilance and stimulates him to controversial thinking. One should have leisure for this experience – actually, one should retire, like the 20 distinguished authors, to a chalet in the Laurentian Mountains for the sole purpose of enjoying a scientific feast.

Basically, this is a collection of contributions utilizing the concept of the reticular system of the brainstem and diencephalon to interpret states of consciousness, the latter most readily illustrated by sleep and wakefulness. The discussion of the guests is given verbatim. Here the reader will be presented with the authors' integrated investigative work, sparing him much of the effort of thumbing through the detailed publications of Jasper, Magoun, Moruzzi, Olszewski, Nauta, Whitlock, Hess, Bremer, Brazier, Fessard, Adrian, Gastaut, Penfield, R. Jung, Grey Walter, Hebb, Lashley, Kubie, and Rioch.

The reviewer, swept on somewhat by the forthright spirit of the book, would like to add a litte more fuel to the controversial fire. He was particularly impressed with the presentation of Jerzy Olszewski who, in discussing the cytoarchiture of the human diencephalon, sets down the following propositions: "1) Anatomically, the reticular formation is a poorly-defined structure; 2) the anatomical and physiological conceptions of the reticular formations do not correspond with each other." This blunt statement of an unbridged but not, we hope, unbridgeable chasm, seemed particularly defiiant, and one recalls another somewhat similar statement which characterized the long controversy of Ramon y Cajal with the reticularists. In *Recollection of My Life*, pages 336-337, Cajal remarks: "It has rightly been said that the reticular hypothesis, by dint of pretending to explain everything easily and simply, explains absolutely nothing; and, what is more serious, it hinders and almost makes superfluous future inquiries regarding the intimate organization of the centres. Only by dint of evasions, irrelevancies, and subterfuges could this conception (which, moreover, was upheld almost exclusively by Golgi and his immediate disciples) be adapted to the exigencies of physiology, where the doctrines of reflexes, instinctive actions, functional location in the cerebrum, etc., demand imperiously the recognition of perfectly circumscribed paths or channels of conduction through the cerebrospinal axis."

It is hoped that many will enjoy this outstanding series of contributions and, in the spirit of the symposium, accept its challenge to free and open discussion.

A R. V.

Actos y Trabajos del VI Congreso Latino-Americano de Neuro-Cirurgia

Transactions of the Sixth Latin-American Congress of Neurosurgery. Imprenta Rosgal Hilario Rosillo, Egido 1824, Montevideo, Uruguay. 1387 pages.

FOR THE PAST TEN YEARS the Central and South American countries have held a Congress of Neurosurgery every two years. In reality this is more than a congress of neurosurgery in the strict sense of the word, for its members and attendants comprise practically all of the neurologic talent of the Central and South American countries, and the speakers include both neurologists and neurosurgeons without distinction as to whether the author is primarily a diagnostician or operator. The most recent volume of the transactions of the sixth Latin-American congress of neurosurgery, which was held in Montevideo, March 21 to 24, 1955, was dedicated to Professor Alejandro H. Schroeder who was professor of neurology of the University of Montevideo and whose untimely death a year before the congress deprived South America of one of its real leaders in the field of neurology and neurosurgery.

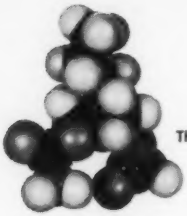
In format the Latin-American congresses have been modeled after most of the European meetings in that themes are taken and discussed by representatives of each of the countries. For the 1955 session the official themes were "Cisternal Hernias," "The Surgery of Pain," "Dyskinesias," and a symposium on "The Thalamus." It would be impossible to review the material in this tome in a short discussion. However, it should be noted that not only were the South American countries represented in the discussion of these themes but also the European countries and the United States.

The reviewer has had an opportunity of attending two previous congresses and has noted in the decade in which these congresses have been held the steady progress in both clinical and scientific aspects of neurologic surgery in South America. Although the majority of the papers were of a clinical nature, there were several excellent presentations of more basic research given by members from South America. One should particularly note the fine studies of the submicroscopic organization of the thalamus by H. Fernandez-Moran, who is now director of the Neurological Institute in Caracas, Venezuela.

The efficient organization of this congress and its volume of proceedings is shown by the fact that the book was published within six months of the actual meeting. The editors of the volume also have gone to considerable trouble to put together on each of the themes a bibliography which should be of considerable value to anyone interested in reviewing the literature of cerebral herniations, surgery of pain, the dyskinesias, or the thalamus. Finally, for those who might be interested in knowing the names and addresses of South American neurologists and neurosurgeons, there is appended to the book a list of the members of the congress with their addresses.

For those physicians who have some knowledge of Spanish, this book should prove to be very interesting and to give a very good summary of the existent knowledge in the fields which were presented. Moreover it indicates the level to which neurology and neurosurgery have now risen in the South American countries. This large volume is heartily recommended to all neurologists and neurosurgeons. For those who may be interested in learning at first hand the state of neurology in South America, the next congress will be held in Medillon, Colombia, probably in May 1957, under the presidency of Dr. Ernesto Bustamente Azuleta.

A. E. W.



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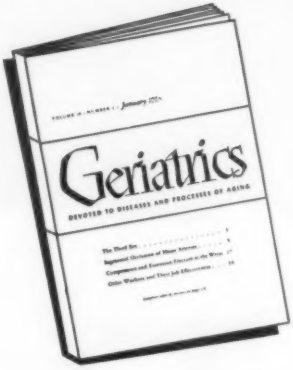

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JUNE, 1956

AAN Meets in St. Louis In the bustle of the Sheraton-Jefferson Hotel in St. Louis, the American Academy of Neurology held its eighth annual meeting, the largest in its history, (April 23-28)....The gong for initiation of program activities was sounded on Monday, April 23, when the annual series of AAN special review courses began with a record-breaking registration of 386. The hum of activities continued to mount as the AAN standing committees went into sessions (Tuesday and Wednesday) and became highly pitched for the Early Bird Party on Wednesday evening, April 25....The scientific sessions, comprising a symposium on the pyramidal tract and 40 scientific papers on problems of current interest in clinical and basic neurology, which had been carefully selected by Program Chairman James L. O'Leary and his associates, extended from Thursday morning until Saturday noon (April 26 to 28). The reading of scientific papers was supplemented by a galaxy of 23 scientific and 11 technical exhibits -- all well chosen and arrayed by the exhibits subcommittee chairman, Benjamin Boshes. Three of the scientific exhibits were motion pictures: Parkinson-like Syndrome in Reserpinized Monkeys (William F. Windle and associates), Babinski Sign (Max H. Weinberg), Posterior Parietal Lobe Lesions in Trained Monkeys (P. Glees and J. Cole), The Diagnosis and Management of Myasthenia Gravis (K. E. Osserman). Also, two program exhibits were presented by the National Society for Crippled Children and Adults and the National Multiple Sclerosis Society....The annual banquet was held on Friday, April 27th, where dancing followed a few brief speeches, including remarks by President Klingman on the skill of Franklin O. Meister and his co-workers in directing and executing flawlessly the complex activities of the registration committee....Honor guests at the head table included Sir Charles Symonds of the National Hospital, Queen Square, and Edwin G. Zabriskie of New York ....For the success of the meeting, congratulations are in order for Frederick L. Stone, general program chairman and coordinator, and to the subcommittee on local arrangements under the co-chairmanship of Joseph J. Gitt and Irwin Levy and their associates, Leonard Berg, Warren Kempinsky, William M. Landau, Walter L. Moore, Herbert E. Rosenbaum, and Louis L. Tureen.

Neurochemistry Scores Success As Special Course Presented for the first time as an AAN special course, neurochemistry received unanimous acclaim at the St. Louis meeting. Under the chairmanship of Maynard M. Cohen, and with a faculty which included Oliver Lowry and Donald B. Tower, the course presented the basic aspects of cerebral chemistry, correlations of chemical changes with clinical syndromes, and discussions on the place of histo- and cytochemical technics as applied to the nervous system....Another successful teaching innovation was a course on common neurologic syndromes designed for general practitioners, which was enthusiastically attended and applauded by 65 general practitioners from the St. Louis area....Preliminary plans for the special courses in 1957 will be announced in the near future.

Symposium of Inquiry on Pyramidal Tract The second symposium of inquiry, sponsored by the AAN research committee, under the chairmanship of Augustus S. Rose, was held at the St. Louis meeting, Thursday evening (April 26). The subject: What We Need to Know About the Pyramidal Tract. After introductory remarks by Dr. Rose, four eminent scientists summarized current knowledge on the subject and emphasized areas where more research is needed from the standpoint of their specialized fields: Arthur M. Lassek (neuroanatomy), Clinton N. Woolsey (neurophysiology), Benjamin Boshes (clinical neurology), and A. Earl Walker (clinical neurophysiology and neurosurgery). Following the summary, questions from the floor ensued until the late hours of the night.

Gala Preview Party of Children's Art Bazaar A sequel to the Early Bird Party was the opportunity afforded Academy members, their wives, and guests to attend a buffet supper preview party of the Children's Art Bazaar at the Famous Barr and Co. Exhibition Hall. On exhibit were paintings by children of many countries, while St. Louis artists were on hand to sketch the guests. In the words of Mrs. James L. O'Leary, chairman of Woman's Auxiliary committee on local arrangements and former chairman of the Art Bazaar, "We were so delighted to have 66 members of the Academy and their wives attend the preview -- their presence added much to the party."....The proceeds from the Children Art Bazaar were given to the Delta Gamma Pre-School Visually Handicapped Foundation.

Woman's Auxiliary Activities A highlight of the Woman's Auxiliary program was the joint luncheon with members of the Academy held Thursday, April 26. Guest speaker was Dr. Kenneth McFarland, education consultant to General Motors Corporation, a nationally known educator, outstanding lecturer, and according to President Klingman: "the most

extensive airline traveler in the world." He addressed the group rather informally, in anecdotal style, using as his theme the importance of service to one's fellow man as a measure of success, rather than material gain....Also featured on the Auxiliary program were a card party, a tour of the famous Shaw's Gardens, and a showing of the movie "Preface to a Life," with commentary by Dr. Dwight M. Palmer of Columbus, Ohio.

* * * * * *

Conference Held on Training in Clinical Neurology On April 23, under the auspices of the National Advisory Neurological Diseases and Blindness Council, a conference was held on training in clinical neurology in the Sheraton-Jefferson Hotel in St. Louis. With A. B. Baker presiding, the delegates to the conference were composed of program directors of the NINDB graduate training grant program in clinical neurology, medical school deans, and noted teachers....Following introductory remarks by the presiding chairman the morning session was devoted to an exposition of needs in neurology by Pearce Bailey, discussed by H. Houston Merritt; accomplishments of the NINDB graduate training program by Russell N. De Jong, discussed by Oliver H. Lowry, Dean, Washington School of Medicine; influence of graduate training programs in neurology on undergraduate medical education by Francis M. Forster, discussed by Alphonse R. Vonderahe; and the administration of NINDB training programs by Gordon Seger. A commentary on the morning session was given by George Aagaard, Dean, School of Medicine, University of Washington....The afternoon was devoted to a panel discussion on "Problems Encountered in Neurological Education," with A. B. Baker as moderator....Besides those already mentioned, also present were 33 program directors and nine other medical school deans: James W. Colbert (St. Louis University), John T. Cuttino (South Carolina), Harold S. Diehl (Minnesota), Stockton Kimball (Buffalo), Philip Price (Utah), Gordon H. Scott (Wayne University), Aura E. Severinghaus (Columbia University), Samuel Trufant (Cincinnati University), and Harold C. Wiggers (Albany).

ANA to Meet in Atlantic City The American Neurological Association will hold its eighty-first annual meeting at the Hotel Claridge in Atlantic City (June 18-20). The The scientific sessions will begin Monday morning, June 18, with the presidential address by Johannes M. Nielsen, and will continue until noon, Wednesday, April 20; a total of 44 scientific papers are to be presented....The annual dinner for association members and guests will be on Tuesday evening, June 19....all communications relating to the meeting should be addressed to the Secretary, Dr. Charles Rupp, 133 South 36th Street, Philadelphia 4, Pa.....Preceding the ANA meeting, also at the Hotel Claridge,

are the meetings of the American Electroencephalographic Society (June 15-17), the American Association of Neuropathologists (June 16-17), and a symposium on cytopharmacology, John L. Nurnberger, Chairman, on Sunday, June 17.

New Board Diplomates in Neurology As a result of examinations of the American Board of Psychiatry and Neurology, held in Philadelphia (April 16-17), 16 candidates were certified in neurology. The successful candidates are: Thomas Louis Auth, Washington, D. C.; Robert Norton Baker, San Antonio; James Arthur Bastron, Mayo Clinic, Rochester, Minn.; Arthur William Epstein, New Orleans; Bill Charles Garoutte, San Francisco; Alexander S. Hartman, Wood, Wis. (supplementary certification); Thomas Richards Johns, II, Charlottesville, Va.; Geraldine King, Philadelphia; Lowell W. Lapham, Shaker Heights, Ohio; Irving M. Levine, Dorchester, Mass.; Charles Nelson Luttrell, Jr., Baltimore; Luigia Norsa, New York City; Iris Fletcher Norstrand, Brooklyn (supplementary certification); Fred Plum, Seattle; Richard Penrose Schmidt, Seattle; and Thomas B. Summers, Iowa City....The October 1956 examination, to be given in Chicago, has been cancelled. The next examinations as now scheduled are: New York City, December 10 and 11, 1956; New Orleans, March 18 and 19, 1957.

Briefs Prof. Robert Paul Bing, noted neuorologist and author of Basle, Switzerland, died of a heart attack on March 15....Prof. Dr. Georges Schaltenbrand, director of the neurological clinic, University of Wurzburg, recently completed a coast to coast lecture tour in the U. S. Returning from California, he stopped in Chicago to give the 31st Lewis Linn McArthur Lecture of the Frank Billings Foundation of the Institute of Medicine, on "Multiple Sclerosis"; also in Chicago he spoke on "Normal and Pathological Studies of Cerebrospinal Fluid Flow," under the sponsorship of the Chicago Neurological Society and the Leo A. Kaplan Memorial Lectureship of the Phi Delta Epsilon Foundation....H. Houston Merritt and Arnold P. Friedman recently participated in a symposium on headache in Los Angeles.... Appearing as witnesses before the Senate subcommittee on appropriations for NINDB were: Cornelius H. Traeger, Augustus S. Rose, Alson E. Braley, and Mrs. Ed W. Johnson, a member of the NINDB Council....Nathaniel W. Winkelman, noted neuropathologist and neurologist, member of the AAN, died at his home in Philadelphia, February 13....

Percy Bailey

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Composition: Each tablet contains extracts of rhubarb, cascara, precipitated sulfur, peppermint oil and fennel oil, in an activated charcoal base. Action and Uses: Mild laxative, adsorbent, carminative and a purifier. For use in indigestion, hyperacidity, bloating and flatulence. An excellent detoxifying substance with a wide range of uses in dermatology. Administration: 1 or 2 tablets daily ½ hr. after meals. SUPPLY: Tins of 100.

SEDATIVE AND EUPHORIA FOR NERVOUS, IRRITABLE PATIENTS
VALERIANETS-DISPERT®
TASTELESS, ODORLESS, NON-DEPRESSANT SEDATIVE & EUPHORIC
Each Chocolate Coated Tablet Contains Ext. Valerian (highly concentrated) 0.05 Gm. dispergentized finely subdivided for maximum efficiency.
Indicated in cases of nervous excitement and exhaustion, anxiety and depressive states, cardiac and gastrointestinal neuroses, menopausal and menstrual malimema, insomnia.
Dose: 1 or 2 tablets t.i.d. supply Bottles of 50, 100, 300 tablets.

A MODERNIZED METHOD FOR PREPARING BUROW'S SOLUTION U.S.P.
PRESTO-BORO®
In Tablets or Powder in envelopes (ALUMINUM SULFATE and CALCIUM ACETATE)
FOR USE AS AN ASTRINGENT and TOPICAL DRESSING
(U.S. Pat.)
Dissolve in plain water as directed for preparing astringent Burow's Solution for treatment of Swellings, Inflammations, Sprains. Antipruritic, decongestive action. Accurate uniform dosage. Stable, Lead free.

FOR PULMONARY CONDITIONS
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3% solution Quinine with 2½% Camphor for Intramuscular Injection

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PERSISTIN — LONG-ACTING PAIN RELIEVER

Persistin is a combination of a comparatively soluble, quickly absorbed ester of salicylic acid (acetylsalicylate) and an ester (salicylsalicylate) which is insoluble in gastric secretions, resulting in delayed absorption. Its use is indicated for the relief of pain and distress during hours of sleep; arthritic and rheumatic involvements, bursitis, myalgias, neuralgias, and other types of pain relieved by salicylates; fever and distress of upper respiratory and other infections. Analgesic levels of salicylate persist in the blood for five to eight hours following a single dose. The tablets are made by Sherman Laboratories, Detroit, Michigan.

NEW DRUG FOUND TO CALM AGITATED PATIENTS

A new drug which calms and controls acutely agitated mental patients, alcoholics, and drug addicts and facilitates their physical and psychiatric rehabilitation has been disclosed at a recent medical staff conference of the District of Columbia General Hospital. The new drug differs from others in use in that the calming of patients is not masked with depression. Little or no fall in the patient's blood pressure has been observed. , Vasomotor collapse has not occurred, nor has the drug produced tachycardia. There is no evidence of intolerance to intramuscular nor intravenous administration of the drug, no pain on injection, and no tissue destruction at the site of injection. Jaundice and agranulocytosis attributable to some drugs in the field of chemotherapy has not been observed thus far after administration of the new drug.

The drug, which is still undergoing extensive clinical testing, has been developed by Wyeth Laboratories and is known as Sparine, or in the laboratory as WY-1094. Sparine (promazine hydrochloride) is a phenothiazine derivative .It has been found to control effectively symptoms of central nervous system excitation and to calm the acutely agitated patient. It is indicated in the management of a variety of acute mental disturbances, including such alcohol-induced syndromes as delirium tremens, acute hallucinosis, acute tremulousness, and inebriation, as well as agitation due to various psychoses and withdrawal symptoms of drug addiction.

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POCKET-SIZE SUCARYL SOLUTION

Users of Sucaryl sweetening solution may now carry their sweetener wherever they go in a new refillable pocket or purse container introduced by Abbott Laboratories, North Chicago, Illinois. The leak-proof half-ounce plastic squeeze bottle holds approximately a week's supply of Abbott's non-caloric sweetener in solution form. The new bottle is easily refilled from either the four-ounce or pint bottle of Sucaryl solution and is available at pharmacies and in drug sections of department stores.

FRENQUEL IN ALCOHOLISM

Sixteen patients out of 19 treated for acute alcoholic hallucinosis (the "DT's") were completely relieved of their hallucinations soon after administration of Frenquel, according to a recent report from two Winston-Salem, North Carolina hospitals. Frenquel is a product of the Wm. S. Merrell Company, Cincinnati.

Physicians cited an example of a 46 year old man whose family claimed he had been an alcoholic for 20 years. During the week prior to entering the hospital, he had consumed a bottle of whisky a day. He was acutely intoxicated and complained that airplanes were in the room swooping at him. He had lost track of time and place. He was given Frenquel, and within 30 minutes he was oriented and no longer disturbed. He was hospitalized for four days for general medical care, but there was no recurrence of his delusions or hallucinations.

CYTOFERIN RELEASED BY AYERST

Presented as the direct approach to greater iron absorption and the logical combination in treating hypochromic microcytic anemia, "Cytoferin," providing ferrous sulfate and vitamin C, has been released by Ayerst Laboratories, New York. Each "Cytoferin" Tablet contains: ferrous sulfate exsic (3 gr.) 200 mg.; and vitamin C (ascorbic acid), 150 mg.; available in bottles of 100 and 1,000.

FLEXIN: A NEW PRODUCT

McNeil Laboratories, Inc., Philadelphia, is now in full production on a new product. It is generically zoxazolamine, a newly synthesized compound unrelated to any available agent, and has been found effective orally for the relief of muscle spasm in musculoskeletal and neurological disorders. These include low back pain, fibrositis, spondylitis and rheumatoid arthritis; and spinal spasticity states, cerebral palsy, multiple sclerosis, cerebral vascular accidents and Parkinson's disease.

A "lissive" agent, Flexin eliminates skeletal muscle spasm without interfering with normal muscle power or activity.

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ARTANE is supplied in 2 mg. and 5 mg. tablets, and as an elixir containing 2 mg. per teaspoonful (4 cc.) Dosage: 1 mg. the first day, gradually increased, according to response, to 6 mg. to 10 mg. daily.

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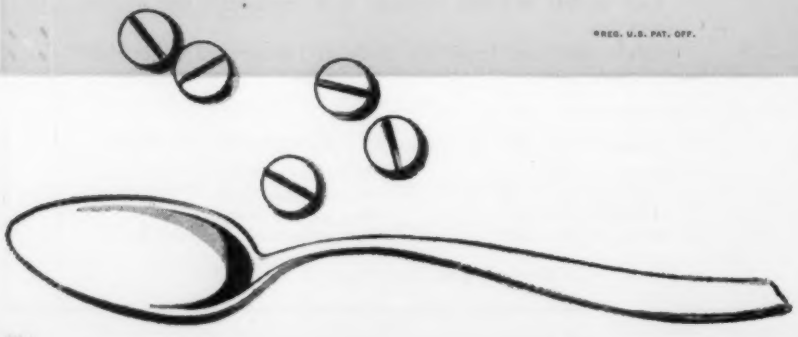

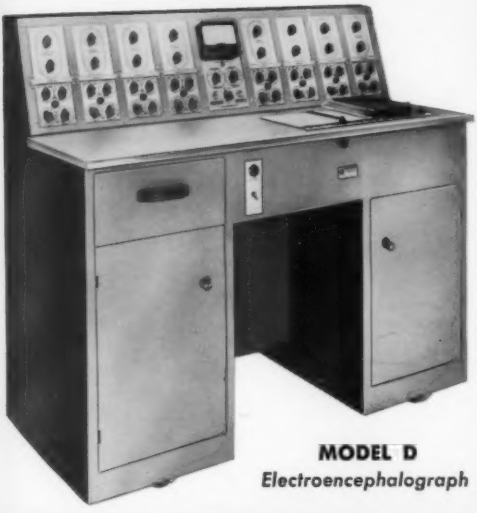

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Aspirin	200 mg.	(3 grains)
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Caffeine	30 mg.	(½ grain)
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Adult dose: 1 or 2 tablets up to four times daily.

Bottles of 100 tablets. *Narcotic blank required.*

"Such a combination has proven clinically to be far more effective and no more toxic than equivalent doses of any of these used singly."[1]

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Demerol, brand of meperidine, trademark reg. U.S. Pat. Off.

[1] Bonino, J.J., and Backup, P.H.: *Northwest Med.*, 54:22, Jan., 1955.